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UDC 612.273

Enhancement of Human Tolerance of Acute Hypoxia by Adaptation and Intense Training at High Altitudes

18400067c Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 14 No 3, May-Jun 88 (manuscript received 4 Jun 85) pp 441-445

[Article by A. Yu. Katkov, deceased, Moscow]

[Abstract] A comparative analysis was conducted on tolerance of acute hypoxia by mountain climbers (74 males) and non-climbers (48 males), the latter subjected to adaptation and/or 3 days of intensive training under pressure chamber conditions (5000 to 9000 m). Pressure chamber studies showed that the mountain climbers residing in subalpine areas tolerated an altitude of 9700 +/- 170 m for 56 +/- 2.2 min before mental clouding 5-6 months after the last climb. The corresponding parameters for mountain climbers residing in lowland areas were, respectively, 9200 +/- 150 m and 50 +/- 1.2 min. Maximum tolerance of the non-climber controls reached 8300 +/- 100 m, with a tolerance time of 41 +/- 1.0 min at that altitude. A day after the 3-day adaptation/training regimen, the figures improved to 9300 +/- 90 m and 50 +/- min. A 7- to 56-day excursion to elevations of 5621-8848 m by the lowland mountain climber raised their tolerance figures to 9600 +/- 100 m and 54 min; the improved tolerance of hypoxia persisted for some 20 days. Analysis of cardio-vascular function tests and respiratory studies demonstrated that after adaptation to high altitudes in a pressure chamber set at 9000 m the coefficient of oxygen utilization in the climbers was higher than in the nonclimbers subjected to the 3-day regimen. References 7 (Russian).

UDC 577.352.335

Biochemical Approaches to Investigation of Potential-Dependent Sodium Channels

18400031c Yerevan NEYROKHIMIYA in Russian Vol 7 No 1, Jan-Mar 88, pp 126-141

[Article by V. K. Lishko and N. G. Gimmelreykh, Institute of Biochemistry imeni A.V. Palladin, Ukrainian Academy of Sciences, Kiev]

[Abstract] This article surveys the literature on purification and reconstitution of the potential-dependent sodium channel. The review covers the channel's interaction with toxins that are highly specific for its structural elements (water-soluble neurotoxins, liposoluble neurotoxins, polypeptide toxins, and scorpion, or β, toxins) and the use of such toxins as markers for isolating and purifying sodium channel components. Solubilization of channel components, reconstitution of the channel on vesiculated and flat lipid membranes and on liposomes, chemical composition and subunit structure, and the biogenesis of channel-forming proteins are also discussed. References 82: 9 Russian, 73 Western.

UDC 577.175.853'17:547.964.4.057

Effective Synthesis of Cyclic Bradykinin Analogs

18400032a Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 14 No 3, Mar 88 (manuscript received 7 May 87) pp 299-307

[Article by I. E. Mutule, F. K. Mutulis, D. P. Erglis, D. A. Yakstinya, I. P. Sekatsis, S. Kh. Rozite, V. D. Grigoryeva, I. P. Misinya and G. I. Chipens, Institute of Organic Synthesis, Latvian Academy of Sciences; Experimental Plant of Institute of Organic Synthesis, Latvian Academy of Sciences, Riga]

[Abstract] Cyclic analogs are used to study the molecular structure and mechanism of biological action of bradykinin and kallidin. Cyclic bradykinin and cyclic ε-kallidin are synthesized with new methods that involve closure of the cycle through the proline and phenylalanine groups. The cyclization process is performed in stages by means of pentafluorophenyl ester hydrochlorides. The cycle was formed in a dioxane solution, which is easier to obtain in pure form than dimethylformamide, which was previously used. The yield in the cyclization stage is thus increased to 50-60 percent. The synthesis method allows the use of certain intermediate compounds in the production of cyclic bradykinin for the synthesis of cyclic kallidin, and reduces the use of tert-butyl glycine and proline esters. Figures 3, references 22: 9 Russian, 13 Western.

UDC 547.962:541.63

Comparison of Conformation Capabilities of Bradykinin and IgercinMolecules

18400032a Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 14 No 3, Mar 88 (manuscript received 19 May 87) pp 308-312

[Article by G. V. Nikiforovich, Yu. Yu. Balodis and G. I. Chipens, Institute of Organic Synthesis, Latvian Academy of Sciences, Riga]

[Abstract] The authors have previously suggested that the C-terminal nonapeptide of the ε chain Arg-Ala-Val-Ser-Val-Asn-Pro-Gly-Lys, called igercin, is a potential cytophilic center of the human immunoglobulin E molecule. Here, a computational search for low-energy igercin molecule skeletal structures is performed with a molecular model with rigid valent geometry and trans-conformation of the prolene group; the parameters of the potential functions of atom-atom interactions were used. Electrostatic interactions were considered in a monopole-monopole approximation with a macroscopic dielectric constant of 3.5, which models the situation arising when biologically active peptides bond with a receptor. The computational data indicate that there may be some similarity between igersin and bradykinin molecules at the level of spatial structures. However, the bradykinin molecule structure involved is not among the "biologically active" conformations of the molecule necessary for bonding with specific bradykinin receptors. Igersin, therefore, should not manifest bradykinin-like properties or antagonistic properties in classical tests of the depressor effect in vivo or the myotrophic effect on isolated organs. However, the conformational similarity, in combination with similarity of amino-acid sequences, may cause possible interactions of both molecules with the same type of receptor in other biological tests. Figures 3, references 10: 6 Russian, 4 Western.

UDC 577.175.829'17

Interaction of Cyclic Analogs of Substance P With Rat Brain Membranes

18400032c Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 14 No 3, Mar 88 (manuscript received 15 Jul 87) pp 313-317

[Article by Ye. M. Lazakovich, I. E. Mutule, Yu. N. Utkin and V. I. Tsetlin, Institute of Bioorganic Chemistry imeni M.M. Shemyakin, USSR Academy of Sciences, Moscow; Institute of Organic Synthesis, Latvian Academy of Sciences, Riga]

[Abstract] The undecapeptide substance P is considered a probable peptide neurotransmitter. Some ordered conformation of substance P is thought to be present on phospholipid membranes and to be essential for recognition of the specific receptor sector. Fixation of such a biologically active conformation of the bioregulator via cycle formation could result in the creation of substances

with a number of interesting properties—substances with higher resistance to proteolytic enzymes, for example, or with selectivity or "superhigh" activity. To test this hypothesis, the authors studied the ability of various cyclical substance P analogs to inhibit bonding of ^{125}I-labeled substance-P derivatives with rat brain membranes. Analysis of the bonding of the substance with the membranes revealed the presence of a specific saturating bond. It was found that the chemical nature of the bond closing the cycle is not essential for the activity of the cyclic analog. It is suggested that the relatively low activity of shorter cyclical analogs interacting with brain membranes may result from the absence of the N-terminal molecular fragment. It is noted that there are several types of tachykinin receptors in the central nervous system, the affinity of substance P for which differs by several orders of magnitude. Formation of the cycle may stabilize the substance P conformation which has high affinity for the type of receptor with which it interacts with relatively less efficiency. Figures 3, references 17: 2 Russian, 15 Western.

UDC 577.322.2:541.121

Cooperativeness in Transition of Solubilized Bacteriorhodopsin to Acidic Purple Form Under Influence of Cl^- Anions

18400032d Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 14 No 3, Mar 88 (manuscript received 28 Jul 87) pp 318-320

[Article by A. L. Drachev, L. A. Drachev, A. D. Kaulen and L. V. Khitrina, Moscow State University imeni M. V. Lomonosov, Interdepartmental Scientific Research Problem Laboratory of Molecular Biology and Bioorganic Chemistry imeni A. N. Belozerskiy]

[Abstract] The transition of "neutral" purple bacteriorhodopsin to BR605 is pH dependent. The transition of BR605 to BR565 is determined by the absorption of anions. It has been demonstrated that in a suspension of purple membranes, the transition of BR605 to BR565 does not result from the absorption of a proton, but rather occurs under the influence of anions. Still unanswered, however, was the question as to whether the cooperativeness thus manifested is related to the properties of the individual bacteriorhodopsin molecule or to their interaction in a triad. Laurylsaccharose, the only known detergent that can be used to study conversion of blue and purple acid forms of bacteriorhodopsin to the monomer state, was used here with HCl to study circular dichroism spectra, the standard test for the transition of bacteriorhodopsin from the triad to the monomer state. The conversion of the blue acid form of solubilized bacteriorhodopsin to the purple form in HCl solution was examined, and the cooperativeness in the transition was found to be related to the absorption by each purple membrane bacteriorhodopsin molecule of three Cl^- anions during the transition of BR605 to BR565. Figures 2, references 18: 4 Russian, 14 Western.

UDC 577.113.5

Nucleotide Sequence of Genes of and Subunits of Photobacterium Leiognathi Luciferase

18400032f Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 14 No 3, Mar 88 (manuscript received 6 Jul 87) pp 412-415

[Article by B. A. Illarionov, M. V. Protopopova, V. A. Karginov, N. P. Mertvetsov and I. I. Gitelzon, Krasnoyarsk State University; Institute of Biophysics, Siberian Division, USSR Academy of Sciences, Krasnoyarsk; Institute of Clinical and Experimental Medicine, Siberian Division, USSR Academy of Medical Sciences, Novosibirsk; Novosibirsk Institute of Bioorganic Chemistry, Siberian Division, USSR Academy of Sciences]

[Abstract] Bacterial luciferase is an α, β-heterodimer protein which catalyses in vitro oxidation of reduced flavinomononeucleotide and aliphatic aldehyde and reduces oxygen. Biochemical studies have not answered the question of the significance of the "luciferase shunt" in the metabolism of the bacterial cell and the mechanism of light emission. The authors determined the primary structure of a fragment of chromosomal DNA of the marine bacterium *Photobacterium leiognathi* that they had cloned in an earlier work. The nucleotide sequence of the cloned DNA fragment is presented, revealing two rather long, open counting frames bounded by translation initiation and termination sites. The peptides coded contain 354 and 325 amino acids and have molecular mass 40,375 and 37,377 Da, quite similar to the molecular masses of the α and β luciferase subunits of *P. leiognathi*. The materials obtained help to identify the conservative regions of luciferase, which are important for the functioning of the protein, and allow an approach to a study of the mechanism of action of luciferase by producing directed amino acid replacements. Figures 2, references 8: 3 Russian, 5 Western.

UDC 547.382.3.057:577.112.854

Synthesis and Properties of C13-Dependent Retinals

18400032g Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 14 No 3, Mar 88 (manuscript received 19 Jun 87) pp 421-423

[Article by S. V. Yeremin, B. I. Mitsner, S. V. Danshina and L. V. Khitrina, Moscow Institute of Precision Chemical Technology imeni M. V. Lomonosov; Institute of Biological Physics, USSR Academy of Sciences, Pushchino; Interdepartmental Scientific Research Problem Laboratory of Molecular Biology and Bioorganic Chemistry imeni A. N. Belozerskiy, Moscow State University imeni M. V. Lomonosov]

[Abstract] A method is suggested for producing structural analogs of retinal that are modified in the C13 position. The key stage in the process is the condensation of ketoacetyl with the appropriate Grignard reagents.

The reaction is performed with an excess of organomagnesium compound at 0°C in ether. After decomposition of the reaction mixture with a saturated NH_4Cl solution, the substance is extracted with ether and dried with Na_2SO_4, and the solvent is removed. Increasing the number of H_3C groups at the α carbon atom in the Grignard reagents containing aliphatic substituents increases the fraction of 1,4-attachment product. When all of the aldehydes synthesized were tested in reactions with bacterioopsin, they formed artificial pigments with absorption maxima indicating covalent bonding between retinal analogues and apoprotein, indicating the existence of a cavity in the protein vicinity of the H_3C group at the C13 chromophore group atom of bacteriorhodopsin. References 6: 2 Russian, 4 Western.

UDC 577.150.3+577.156

Isolation and Purification of Clostridium Perfringens Phospholipase and Phospholipase Specific Antibodies on Biospecific Polymeric Adsorbent

18400054a Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 24 No 3, May-Jun 88 (manuscript received 17 Jul 86) pp 305-309

[Article by G. F. Shemanova, T. M. Postnikova, V. V. Chupov, L. I. Valuyev and N. A. Plate, State Scientific Research Institute of Standardization and Control of Medicinal Biological Preparations imeni L. A. Tarasevich, USSR Ministry of Health; Moscow State University]

[Abstract] Phospholipase C (PLC) of Clostridium Perfringens (α-toxin) is used in preparation of reagents for diagnosis and prophylaxis of gas gangrene. The goal of the present work was to synthesize a polymeric biospecific adsorbent for isolation of PLC and its antibodies. This adsorbent was obtained by radical copolymerizaton in an aqueous solution of acrylamide, methylenebisacrylamide and a specific substrate PLC acetylated with acrylic acid chloride: lecytovitelline of chicken yolk. Maximal adsorption of PLC was observed in presence of an enzyme activator. The residual activity of PLC on the adsorbent was used in isolation of homologous antibodies from the Antiperfringens serum. PLC and PLC-specific antibodies were serologically pure (by the agar precipitation test with the anti-perfringens serum and the primary PLC concentrate respectively). In PAAG electrophoresis, these antibodies gave practically a single zone. Highly purified PLC preparations will be useful in studies of the structure and functions of membrane phospholipids. Figures 2; references 14: 12 Russian (1 by Western author), 2 Western.

UDC 577.352.5:615.919

Action of Argiope Lobata Spider Venom and Its Components on Binding of L[^{3}H]Glutamate with Locust Muscle Membrane

18400054b Kiev UKRAINSKIY BIOKHIMICHESKIY ZHURNAL in Russian Vol 60 No 3, May-Jun 88 (manuscript received 15 Sep 87) pp 78-81

[Article by P. B. Usmanov, A. K. Tonkikh, N. G. Shadyyeva, A. A. Sadykov and B. A. Tashmukhamedov, Institute of Physiology, UzSSR Academy of Sciences, Tashkent]

[Abstract] Two components were previously isolated from Argiope Lobata spider venom: M_m kDA and Mm636 Da, the first blocking Glutamatergic nerve-muscular synapses, the second repressing nerve-muscular transmissions. In an attempt to elucidate the mechanisms of action, the effect of these components on receptor binding L[^{3}H]Glutamate with membranes isolated from locust muscles was studied. Fractionation of the venom over Sephadex 76 yielded two components. One of them (5kDa and higher) blocked synaptic transmission and inhibited binding of L[^{3}H]Glutamate and the other (less than 5kDa) blocked synaptic transmission but did not affect the Glutamate. Thus, at least two components with different mechanisms of action were found in the spider venom. Figures 3; references 6: 2 Russian, 4 Western.

UDC 577.151.042

Polyvalent Metal Salts as Inhibitors of Photochemical Reactions of Bacteriorhodopsin

18400054c Moscow BIOKHIMIYA in Russian Vol 53 No 4, Apr 88 (manuscript received 23 Apr 87) pp 663-667

[Article by L. A. Drachev, A. D. Kaulen and L. V. Khitrina, Laboratory of Molecular Biology and Bioorganic Chemistry imeni A. N. Belozerskiy, Moscow State University]

[Abstract] Lanthanum ions retard relaxation of the intermediate M_{412} in the photochemical cycle of bacteriorhodopsin, this effect being pH-dependent. Lanthanum ions interact only with cytoplasmic surface of the molecule, which made it possible to use them as a test agent for the degree of orientation of bacteriorhodopsin molecules in proteoliposomes. The goal of the present work was to compare retardation of the relaxation of M_{412} by various metal ions: lutecium, aluminum, zinc and iron. The pH- and concentration- dependence was related to the nature of the inhibiting cations; the pH range for effective action of those cations was a function of the salt hydrolysis. Comparison of the effect of aluminum and lutecium salts showed that strong complex forming agents are active even at low concentrations. Figures 5; references 28: 11 Russian (2 by Western authors), 17 Western (5 by Russian authors).

Rhodopsin Photooxidation: Oxygen Consumption and Action Spectrum

18400060b Moscow BIOFIZIKA in Russian
Vol 33 No 3, May-Jun 88 (manuscript received 15 Jul 85; in final form 15 Jul Dec 86) pp 452-455

[Article by A. V. Starostin, I. B. Fedorovich and M. A. Ostrovskiy, Institute of Chemical Physics, USSR Academy of Sciences, Moscow]

[Abstract] In order to further define the mechanism of light-induced retinal damage, in vitro studies were conducted with rhodopsin photo-oxidation using Rana temporaria retinal preparation. Illumination of a suspension of outer segments with light in the 350-500 nm band of the spectrum showed identical action spectra for rhodopsin sulfhydryl groups and lipids. Maximum photooxidation of the SH groups was obtained at 380 nm, with virtually no effect at wavelengths higher than 450 nm. The existence of a single maximum wavelength for both the lipids and the protein indicates that the reaction is mediated by the same sensitizing agent, with the value of the wavelength (380 nm) pointing to retinal. Evaluation of dose-effect parameters showed that the threshold value at 380 nm for oxidation of the SH groups of rhodopsin is approximately 0.1 J/cm development^2. Oxygen consumption studies in the course of photooxidation demonstrated that approximately 25 M O_2 are required for the formation of 1 M malonic dialedehyde, and about 0.3 M 0_2 for the oxidation of 1 M SH groups. Photooxidation studies with a model system consisting of retinal + cysteine combination indicated that ca. 0.01 M 0_2 was needed for the oxidation of 1 M SH groups. The low oxygen requirements for the oxidation of rhodopsin suggest that the oxidation of the SH groups into S-S bonds proceeds with direct involvement of photoexcited retinal, without involvement of singlet oxygen. Figures 2; references 10: 8 Russian, 2 Western.

UDC 612.017.1.014.2-083.224:575.222.75

Dynamics of Immunoglobulin Synthesis and Secretion by Mouse Hybridoma Cells

18400029e Moscow IMMUNOLOGIYA in Russian No 1, Jan-Feb 88 (manuscript received 22 Jan 87) pp 62-65

[Article by O. S. Morenkov and Yu. A. Mantsygin, Institute of Biological Physics, USSR Academy of Sciences, Pushchino]

[Abstract] The dynamics of IgG synthesis and secretion by hybridoma Hλ 14.34.2 were evaluated for a better understanding of the factors underlying monoclonal antibody production. The hybridoma was derived by fusion of SP2 myeloma cells with splenic cells of BALB/c mice immunized with phage lambda. The data showed that, in addition to complete IgG (H_2L_2) molecules, the cells also secreted partially-assembled molecules (H_2L, HL, L_2) and individual chains (H and L). The complete molecules accounted for 80 percent of the total secreted immunoprecipitated activity. The monoclonal IgG represented 15-20 percent of the total quantity of protein synthesized by the hybridoma, and 50-70 percent of the total secreted protein. Continuous ^{3}H-leucine labeling studies showed that radiolabeled IgG appeared within 10 min of label addition and reached an intracellular saturation level in 3 to 3.5 h. Secretion started within 30 min of label addition and increased to a plateau in 2 to 2.5 h. Pulse labeling (5 min) studies demonstrated that half of the labeled IgG is secreted in ca. 1.5 h, while all of the newly synthesized IgG is secreted after 3 h. The latter suggests none or very limited intracellular degradation of the monoclonal antibodies. The kinetic data for the hybridoma cells displayed general similarities to normal and myeloma cells. However, the kinetics of antibody secretion are closer to those of myeloma cells than normal lymphocytes. Figures 3; references 10: 1 Russian, 9 Western.

Biotechnology Trends

18400046 Riga SOVETSKAYA LATVIYA in Russian 14 Sep 88 p 2

[Article by M. Beker, director RMNT [not further identified] "Latviyas Biotekhnologiya," academician, Latvian SSR Academy of Sciences]

[Abstract] Industrialization of agriculture resulting from rapid development of biotechnology led to many improvements in crops but has also brought some new ecologic problems. In Latvia, areas with ecological difficulties include the areas of Yurmala, Sloka, Olayne, Davgava, Gavya, Riga Bay, threatened with darkening potatoes, nitrates in cucumbers and in lettuce, viral particles in tap water, etc. Biotechnology, recognized as the principal factor directing science and technology, is capable of solving a number of global ecologic problems: diagnosis of various disturbances in the ecosystem, development of preventive measures, improved technology for water purification, etc. It could help protect a threatened environment from pollution, could help in maintaining soil productivity, increase the yield of food products without the application of dangerous chemical and so on. Work in this area could be even more important than work in medicine where biotechnology is now well entrenched. A scientific-technical complex is being projected for the preparation of agents and measures aimed at environmental protection. One of the first steps to be undertaken is to reshape thoroughly the agricultural production, change the philosophy of the farmers, the agriculture experts and the administrators. The new stress should be on converting from the popular chemical measures to organic farming. This cannot be done overnight but must be started now. Cellular and genetic engineering methodology could help in lowering the consumption of toxic chemicals. At first, all greenhouse growing should be converted to organic fertilization and to biological protective measures. This should be stimulated by financial rewards if necessary.

UDC 57.088.2:543.545

Microbial Spore Electrophoresis for Isolation of Efficient Industrial Microorganism Strains

18400059b Moscow BIOTEKHNOLOGIYA in Russian Vol 4 No 3, May-Jun 88 (manuscript received 18 Nov 86) pp 335-339

[Article by Yu. I. Shishkov, All-Union Scientific Research Institute of Biotechnology, Moscow]

[Abstract] Studies were conducted with electrophoresis as a means of ready isolation and identification of efficient antibiotic-producing micro-organisms. The experimental studies utilized a tris-borate buffer, pH 8.4, and a 40 to 80 percent sucrose density gradient. Approximately 10^8 microbial spores were introduced into the electrophoretic chamber, with separation conducted under a 10 mA current. The results demonstrated a direct correlation between the electrokinetic potential of the spores and antibiotic production, with the strains showing the greatest electrophoretic mobility exceeding parental strains by 15-25 percent in terms of antibiotic production. This approach to the isolation and identification of highly productive strains was applied successfully to the following general: Bacillus circulans 31, Aspergillus foetidus M-45, Methanobacillus kuzneceovii, Actinomyces fradiae 17, and Actinomyces fradiae S-5-6. Figures 2; references 10: 9 Russian, 1 Western.

UDC 577.112.083.3:628.51

Immunochemical Determination of Air-Borne Yeast Proteins

18400059c Moscow BIOTEKHNOLOGIYA in Russian Vol 4 No 3, May-Jun 88 (manuscript received 31 Oct 86) pp 373-376

[Article by A. V. Yermolayev, I. A. Gukasyan, V. Ya. Ilyina, N. G. Markelova and V. I. Ogarkov (deceased), All-Union Scientific Research Institute of Biotechnology, Moscow]

[Abstract] An immunochemical analysis was conducted on saline extract of Candida maltosa VSB-569 and

VSB-777 surface antigenic complex for comparison with the yeast proteins detected by passive hemagglutination at C. Maltosa processing plants. Fractionation of the antigenic complex on DEAE-cellulose columns yielded 8 protein fractions eluted with 0.2 to 0.2 M NaCl. Each of the fractions yielded lines of precipitation in Ouchterlony plates with antibody against the antigenic complex. In addition, all 8 fractions induced delayed-type hypersensitivity in guinea pigs, with the mean allergenic dose (ED_{50}) ranging from 0.1 to 0.8 μg protein. However, two of the fractions (1 and 2) failed to give positive passive hemagglutination tests. These findings demonstrated that all of the antigenic components of the surface immunogenic complex possess the capacity for inducing delayed hypersensitivity. The date also showed the need for improving the available diagnostic reagents for detection of air-borne yeast proteins to encompass all of the potential allergens released in processing C. maltosa. Figures 1; references 4: 2 Russian, 2 Western.

UDC 663.1:51.001.57

Application of Implicit Functions to Biotechnology

18400059d Moscow BIOTEKHNOLOGIYA in Russian Vol 4 No 3, May-Jun 88 (manuscript received 17 Jun 86) pp 384-389

[Article by S. G. Verdiyev*, I. N. Dorokhov** and Ye. P. Markov***, *Azerbaijan Technological Institute, Kirovabad; **Moscow Institute of Chemical Technology; ***State Scientific Research Institute of Glass, Moscow]

[Abstract] One of the key difficulties encountered in modeling and analyzing biotechnological processes is related to the extreme complexity of the processes, and the fact that all too often only qualitative or subjective information is available. Quantitative relationships are difficult to derive in the case of vague systems, and as a result reliable mathematical models are virtually unattainable. However, the wealth of qualitative data and inferences describing biotechnological processes has led to reliance on implicit functions as a means of relating qualitative and quantitative data and relationships for purposes of construction of mathematical models that depict, with some degree of certainty, biotechnical processes. The initial stage in this approach to bringing order to a multiplicity of variables lies in the qualitative analysis of a system under study, which is most conveniently achieved by formulation of structural diagrams relating various phenomena and effects. specifically, examples are provided of the application of this approach to assessment of grapes used for the production of dry wines and evaluation of the quality of the wine. The success of basing a mathematical evaluation of a process on its linguistic description has shown that the use of implicit functions is applicable to optimization, modeling, and research in biotechnology. Figures 2; references 10 (Russian).

UDC 57.88.6

Determination of Bacillus Thuringiensis Concentration by Laser Turbidimetry

18400059e Moscow BIOTEKHNOLOGIYA in Russian Vol 4 No 3, May-Jun 88 (manuscript received 15 Feb 88) pp 395-396

[Article by M. V. Matveyev and D. S. Shapovalov, All-Union Scientific Research Institute for Design and Construction in Applied Biochemistry, Moscow]

[Abstract] Trials were conducted with a laser-based turbidimetric method for the determination of Bacillus thuringiensis concentration in opaque media, with the results compared with those obtained by the conventional Pasteur-Koch method. The results showed that the laser method yielded concentration values in good agreement with the Pasteur-Koch values, ranging from 3.5 percent differences in ca. 10^3 cells/ml to 13.4 percent at ca. 10^9 cells/m. The key advantage of the use of a laser beam in the turbidimetric determination of B. thuringiensis concentration lies in the fact that it is applicable to opaque solutions. References: 2 (Russian).

Ecological Consequences of Chernobyl Accident Discussed

18400052 Moscow ZNANIYE-SILA in Russian No 8, Aug 88 pp 10-19

[Interview by ZNANIYE-SILA correspondent with Dmitriy Mikhailovich Grodzinskiy, corresponding member of the UkSSR Academy of sciences, head of the Biophysics and Radiobiology Department, Institute of Botany; excerpt from an article titled "Chernobyl: Interview on a Topic of Current Interest"]

[Excerpt] [Question] So what can a person do to withstand the radiation pressure on the population—or can he do anything at all?

[D. Grodzinskiy] Before getting to that topic, I would like to make an important digression. As soon as the Chernobyl accident occurred, the counters in my laboratory indicated an increase in radioactivity right away. At that time, we could only guess what had happened. But instead of explaining to us, the radiobiologists, what had happened, so that we could make recommendations to the public as to the correct things to do in the first few hours after the accident, they sealed our counters. We were told that what had happened in Chernobyl was completely secret.

The people who did this were ignorant, but they were the ones with the authority. An ignorant person always prefers to close his eyes to what is happening, to produce illusion instead of reality. They can tell me that this is all a consequence of the period of stagnation and so on. But then how does one explain that the very same people, while not sealing our counters, nevertheless keep all information concerning the effects of the accident a secret? Why? Where does this wave of instinctive secrecy come from. It has long been time to understand that there must be no secrets in matters of ecology—secrets and ecology are incompatible. Once again, this secrecy comes from unprofessionalism. When the accident happened, I met with more than a few so-called professionals who expounded on catastrophe and made recommendations, without even an idea of what a total radiation dose was! They did not know the stochastic effects of irradiation were.

The secrecy has already had sad results. The brochure "Second Issue of the Internal Report on the Radiation Situation in Finland, May 1986" is here in front of me. Only a few days had elapsed since the accident, and already the Finns were releasing their second bulletin. It explained in black and white what an individual in a contaminated area should do. There were recommendations as to where children could walk; when, how much, and in which regions cows could graze; what to eat, what to drink, and so forth. They put out several such issues. Nothing similar was published in our country, although recommendations along these lines should have been provided to the entire population of the area that was affected. But there, too, a type of "secrecy" was observed. From it came rumors. People began drinking iodine from vials, for example. They burned their mucous membrane.

The fear born from the lack of information, for example, led people to completely stop drinking milk. But milk products are the main source of calcium. People immediately placed themselves in a situation in which they were calcium-deficient, allowing radioactive strontium—which, in its properties and its "behavior" in the body, resembles calcium—to enter the body quickly. Alginates—substances that can help counteract radiation—were needed. And so they sent us all the entire quantity of alginates existing in the Soviet Union—300 grams. But tons were needed. Even in that regard we turned out to be helpless. This is a manifestation of the most thorough unprofessionalism in a field in which the individuals should be highly professional. It turned out to be simpler to keep things secret than to solve the problem. With luck things would be all right. That was how, in theory, those who were to blame for the Chernobyl accident thought.

And here, in my view, the logic is the same. The people have already received the dose, they say, so there is nothing you can do about it, so we need to keep it a secret so there won't be a panic. This is very strange logic, the same that was used when the counters were sealed. And so panic immediately ensues. Kiev is now filled with absurd rumors about what happened and what will happen. It is filled with fear. People have had to go on television to calm the public. But the one leitmotif in these television appearances is that nothing is happening, the situation has improved, the situation is improving, and it will continue to improve more and more, and there are no ecological effects, or almost none.

It seems to me that there aren't any psychologists participating in the preparation of these broadcasts. They would explain that this type of approach to the matter only increases the number of rumors and the mood of panic. Most people do not believe these soothings. In that sense, our approach to the effects is very typical in other countries, too. I recently returned from the Eighth International Congress on Radiation Research. Twelve reports were presented on the problems of the effects of radioactive contamination in Sweden, Switzerland, Finland, France, England, Spain, and other countries, but there was not a single report on our country. This absence of glasnost is especially vexing since there is much more that can and must be done, despite the extraordinary nature of the situation, the uniqueness of the catastrophe, and the absence of precise data on threshold doses and risk factors.

[Correspondent] Dmitriy Mikhailovich, our readers may get the idea that hardly anything has been done to eliminate the effects of the accident...

[D. Grodzinskiy] No. A great deal has been done, and everyone is well aware of that. They have built a sarcophagus and treated enormous territories. The situation has been rectified. But my scholarly duty compels me to speak about the negative side, about what interfered with the work. In any situation, a scholar should speak the

truth. And much still remains to be done to reduce the risk, and much can be predicted theoretically. And if this does not occur, the tragedies of many people and the deformities of the unborn will be on our conscience. The accident should help us, the people of the 20th century, formulate a new, humanistic morality—a morality of responsibility not only for the life of our own generation, but also for the lives of future generations. We won't see these people, but we must remember that they are our children and grandchildren—for whose sake, essentially, we live on this earth.

[Correspondent] What kinds of long-term ecological effects might there be, and how can we overcome them?

[D. Grodzinskiy] Interesting data were recently obtained that make it possible to predict some of the possible ecological effects. Radiation damages DNA. But in the Chernobyl tragedy, processes that are quite different come into play that, however strange, are not associated with the formation of tumors or the appearance of genetic anomalies in descendants. The long-term damage appearing months, years, or decades after irradiation are primarily the result of a disturbance of the endocrine balance. But as surprising as it may seem, certain "ordinary" diseases such as pulmonary inflammations, infarcts (with vascular injury), and nervous disorders develop as a result of these injuries. In some cases, the immune system may be damaged. Incidentally, those are the most likely effects of this type of accident. And some weakening of the immune system is already occurring in a number of individuals.

A great number of dead mice and rats turned up in Kiev just after the accident. This fact is surprising in and of itself. It is known, for example, that right after the explosions on Bikini Atoll, the rats were in rather good health. The level of radioactivity in Kiev wasn't high enough to cause the death of these animals. What happened? Here is the problem I spoke of in the beginning of our conversation—the possibility of predicting the response of the body and solving an equation having many variables. What component gave way in these unwilling test animals? Couldn't this information be used to study the situation as it applies to humans?

These questions have troubled us. It turned out that the animals' deaths were not directly associated with the radioactivity and that mediated response mechanisms were triggered. Radioactive iodine was released during the accident. This iodine, as experiments have shown, accumulated in the thyroid gland, causing a change in its functioning. This affected the hypophysis, which regulates the body's immune response. The animals' immunity was weakened, and they died not of radiation but of the epidemics that had flared up among them.

The same thing can happen with people, but, fortunately, without such tragic consequences. There were no epidemics, but an increase in morbidity was nevertheless observed. The weakening of immunity as an indirect consequence of radiation is now being observed in many contingents of Kiev's residents. The duration of different types of diseases, including pulmonary inflammation, increased, and the flu epidemic was more severe. Physicians complain of a weakening of immunity, and it is entirely possible that this is a result of the accident. But this is nothing catastrophic. There are a great many means for rectifying the situation. Unfortunately, no one is telling the public what to do. And there are indeed simple means that will help bolster the immune system. Vitamins are needed, for example. Many people have virtually stopped eating greens, for fear of radiation. This is completely wrong. Radiation has a stronger effect on a body that is deprived of vitamins.

Now a whole group of problems has emerged that require a scientific solution—specifically, a plan to reduce the total radiation dose. There are, for example, substances called radioprotectors. They strengthen the body's resistance to radiation. Some radioprotectors create an oxygen deficiency in the cell. As a result, the cell divides less vigorously, and the amount of radiation damage is reduced. We know of such substances for acute radiation injury. The problem now is to find radioprotectors for chronic irradiation. This problem is fully solvable. There are different groups of vitamins, peptides, succinic acid, carotene contained in carrots, and a whole other series of compounds. The most effective of the radioprotectors increase radiation resistance approximately twofold.

I want to mention that alcohol consumption increased during the accident. This was because many people knew that ethyl alcohol is also a radioprotector. This is only partly true. The problem is that, although alcohol does indeed increase radiation resistance by a factor of 1.13, it also destroys the molecules of vitamins, which are themselves radioprotectors. Thus, the effect of alcohol is more negative than positive. It is much better to drink carrot juice and other juices that contain carotene. As you see, despite the weakness of the theoretical base and the uniqueness of the accident, radiobiologists can make some useful recommendations.

[Correspondent] Obviously, there are definite ways of reducing the total radiation dose?

[D. Grodzinskiy] Certainly there are. And solving the problem is once more directly related to the problem of glasnost. Announcements are now appearing about the fact that the total dose will faintly decrease. This is completely untrue.

The total radiation dose will, inevitably, increase. Especially in the next few years, a large volume of the radioactive particles will begin to be linked in trophic chains entering human and animal bodies. Hiding this is senseless. It must be acted upon, not hidden. The increase in the total dose may be slowed down primarily with the proper nutrition and the use of substances that block the effect of radiation. I have already spoken about

them. They are radioprotectors. Blocking the ingestion of radioactive particles in trophic chains is a problem of enormous complexity. Much is being done there.

But many problems still remain to be solved. For example, the ingestion of contaminated products from a number of regions located in the western and northern track of the radioactive cloud, i.e., the Narodicheskiy and Polesskiy rayons, is still possible. In my view, industrial crops should be introduced in these territories. Doses of fertilizers and lime should be increased for certain types of soil contamination. For example, cesium behaves toward plants in the same way that potassium does. If potassium fertilizers are added, the entry of cesium into plants may be attenuated in certain conditions. For this reason, great care should be taken with regard to plants' potassium nutrition. Now, strontium is removed by using calcium. Leaf feedings that reduce the intensity of the absorption of radioactive substances can and should be used. This can have a large effect. These simple measures ultimately reduce the total dose.

Unfortunately, however, these problems are being addressed very slowly. Specifically, our laboratory developed a method of using leaf feedings to feed plants that reduced the plants' entrainment of radionuclides. We tested the leaf feedings in the winter of 1986-1987. To get good results with the seeds, we broke up and chopped out the soil blocks with winter wheat, set up the experiements, and studied how the compounds behaved in soil. Timely recommendations were developed as a result, and our laboratory immediately sent the documents to the UkSSR Agroindustrial Association [Agroprom]. The reply, as might be expected, was negative, and it arrived as late as summer, when it was already too late to make leaf feedings. The Agroindustrial Association did not even look to see what kind of leaf feedings were being discussed and why they were necessary. Unfortunately, this is not the only case of a careless attitude toward scholars' proposals.

[Correspondent] What other methods are there, in your view, to reduce the total radiation dose?

[D. Grodzinskiy] First of all, the public must be provided with individual dosimeters, like those used by the Japanese who go to the market equipped with counters and measure the radioactivity of cabbage or fish. I am not saying that we are not monitoring products for radiation, but there is a strong probability of untested agricultural products ending up on the table. Contaminated products, such as mushrooms, may suddenly come from even the most remote regions. The same can happen with water. You can measure the radioactivity level of water, and it will be within the norm, but the sediment in your teapot will be radioactive.

A person must know what he is eating and drinking. Not only do we not have individual dosimetry equipment, but any attempts to manufacture such equipment are considered criminal. People are fired from their jobs to keep them from doing this. The explanation once again is "to keep anything from getting out," to avert a panic. But the fact that absurd rumors are spread from a lack of information and that people's health is being harmed does not seem to worry anyone.

Yes, we still cannot predict with any reliability the ecological effects, but we must at least prevent an increase in the total dose among the population. This much we can do. Owing to a lack of information, people are increasing their own radiation doses. Thus, cases of increased radioactivity in Russian stoves are widespread in rural areas. They began firing the stoves with dry sunflowers that turned out to contain a great quantity of radionuclides.

[Correspondent] Dmitriy Mikhailovich, it is known that a number of specific problems have arisen as a result of the accident. These include psychological, stress-related problems?

[D. Grodzinskiy] Yes, some mentally unstable people have decided that, as they say, "life is finished" for them, that they are lost. Others have sunk into debauchery, while still others have fallen into a depression. In my view, psychologists must generally become indispensible participants in analyzing the effects of the accident. As far as I know, pschological studies are now under way with the group of the population that has been relocated from the 30-kilometer-radius zone. I would say that psychological assistance is extremely important in this situation. People need help in overcoming the stress for which they were unprepared. In this context, physicians should expect an increase in the number of nervous disorders, infarcts, and hypertonias—in a word, in the entire "bouquet" that is blossoming in the soil of high stress.

Another specific problem that, in my view, warrants the attention of the scientific community is that of the ecobiological situation in the 30-kilometer-radius zone. Here, like it or not, a unique experiment has been set up. Man has left. Nature, touched by man's presence, has remained. How are the animals, and the entire ecosystem, getting along there? It is already known that flocks of hens have suddenly formed. Roosters have started to form new families for some reason, and their aggressiveness has increased. Hens and roosters have stopped fearing foxes. Large dog packs have formed that, in structure, resemble wolf packs. Abandoned fields of wheat and barley remain. Crops are becoming part of the natural biosystem, and new, never-before-seen plant communities are springing up. The very process of tamed nature running wild is very curious. Many patterns are emerging here that must be taken into account when the course of events is reversed—the taming of wild nature.

The most unexpected problems are arising. For example, an enormous quantity of ducks has appeared in the Chernobyl region. This is natural. It is quiet there. There

are few people. There is a lot of food. But what is happening is that these hundreds of thousands of ducks are accumulating radioactive substances. They are flying off to all kinds of places in every direction. And, of course, no one would want the public to eat radioactive game. This seems a trifle. But there are no trifles where radiation is involved. And this problem is yet another one where individual testing equipment is necessary.

Detrminations indicate that a large portion of radioactive contaminants have acculumlated in silts. How will they behave when there is heavy flooding? Will they increase the activity level of the water? Will the animal life populating rivers and reservoirs suffer? After all, these are also questions that demand timely theoretical interpretation, followed by some sort of practical measures. Indeed, if silts are deposited in the fields by strong freshets, it will be a catastrophe. Enormous tracts of the most fertile ground will become radioactive.

In a word, new, sometimes completely unexpected problems relating to different fields of knowledge—psychology, medicine, radiology, mathematics, construction—are constantly being identified. And we should not expect the number of such problems to suddenly decrease sharply. The reverse is more likely true. I will emphasize again that these problems should not be hushed up. Glasnost and openness are needed. Secrecy of any kind will only bring harm, because it hides problems and does not give the broad scientific community the opportunity to take part in solving them. The experience garnered in overcoming the effects of the catastrophe must be open not only to us, but also to the whole world.

[Correspondent] What can you say about the communications that have appeared in the special press where, specifically, the following was stated: "The effects of direct radiation on the plant and animal communities in the form of radiation damage to the coniferous forests and noticeable changes in the numbers of soil meso-microfauna have appeared in the restricted zone of heavy radiation contamination extending several kilometers from the Chernobyl AES. No special ecological effects of radioactive contamination have been observed in the rest of the territory that was affected by the accidental release."

[D. Grodzinskiy] Look here. (Dmitriy Mikhailovich took a small photograph from inside the desk.) This was taken far from Chernobyl, outside the zone. What kind of a tree do you think this is?

[Correspondent] Pine, the needles are long...

[D. Grodzinskiy] From the photo, even the most experienced specialist would not say that this is a spruce. The needles are 5 to 6 centimeters each. And this is the result of radiation...

[Correspondent's postscript] P. S. Dmitriy Mikhaylovich game me the entire packet of photographs. You have seen some of them [on the pages of the article].

[Photographs not reproduced.]

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Effects of Tactivin on Expression of Cytoplasmic and Cell Surface Immunoglobulins in B Cells

18400029a Moscow IMMUNOLOGIYA in Russian No 1, Jan-Feb 88 (manuscript received 16 Apr 87) pp 40-43

[Article by T. P. Markova, Institute of Experimental Pathology and Therapy, USSR Academy of Medical Sciences, Sukhumi]

[Abstract] Trials were conducted with the effects of tactivin, an immunomodulator isolated from calf thymus, on the cell surface and cytoplasmic expression of immunoglobulin in B cells of healthy individuals and patients with chronic lymphocytic leukemia and B cell lymphosarcoma. The assessment of the effects in vitro and in vivo were conducted following removal of T cells by the rosette formation technique. In the in vitro series, tactivin, in as low a concentration as 2.5 μg/3 x 10^9 B cells, after 18 h incubation at 4 °C or at 0.5 h at 37°C, led to a statistically significant reduction in cells showing surface expression of immunoglobulins of all classes, concomitant with an increase in the number of cells showing cytoplasmic expression. A less pronounced depression was also observed in the case of B cells derived from control subjects. In vivo studies were conducted with 7 patients with chronic lymphocytic leukemia and 2 with lymphosarcoma treated subcutaneously with 100 μg tactivin per day for 5 days and then once per 10 days for a total of 800 μg of tactivin. In that time frame, the patients were not maintained on any other form of chemotherapy and there were no changes in their clinical state. The results in terms of surface and cytoplasmic expression of immunoglobulins were analogous to the results obtained in the in vitro tests. A decrease in the percentage of B cells with surface expression of immunoglobulin was evident after 5 injections of tactivin, a change that persisted for 3-5 months after a full course of 8 injections. Conversely, the number of B cells with cytoplasmic expression increased after 5-8 injections and persisted for a similar period of time thereafter. These findings were interpreted to indicate that tactivin participated in the differentiation of B cells. Figures 1; references 14: 6 Russian, 8 Western.

UDC 615.371.015.6:[579.222:615.919

Immunologic Properties of Hexa- and Decapeptides of B-Subunit of Enterotoxins

18400029b Moscow IMMUNOLOGIYA in Russian No 1, Jan-Feb 88 (manuscript received 27 Nov 86) pp 49-53

[Article by G. I. Kostina, M. V. Sidorova, N. Yu. Alekseyeva, S. M. Andreyev, L. A. Fonina, I. N. Nikolayeva, G. A. Ignatyeva, and I. G. Sidorovich, Institute of Immunology, USSR Ministry of Health, Moscow]

[Abstract] An analysis was conducted on the immunogenic and antigenic properties of conjugates prepared by coupling hexa- and decapeptides of the B-subunit of cholera toxin to a copolymer (N-vinylpyrrolindone + maleic anhydride). Intraperitoneal and per os immunizations were conducted on a variety of inberd and hybrid mice, and the antibodies tested in in vivo toxin-neutralizing tests and immunoenzyme assays. The data demonstrated that worthy of particular attention, was one conjugate, designated conjugate V (copolymer-$(decapeptide)_{10}$), since it could also be administered orally without undergoing proteolytic cleavage and retaining its immunogenicity. The antibodies formed against conjugate V were active in both tests, and also neutralized E. coli enterotoxin, Polyclonal and monoclonal antibodies against cholera toxin react in vitro with the conjugate, indicating that the conjugate retained the specificity of the native toxin. Figures 7; references 21: 8 Russian, 13 Western.

Modulation and Stimulation of Murine Hemopoietic System by Bacterial Polysaccharide Salmosan

18400029c Moscow IMMUNOLOGIYA in Russian No 1, Jan-Feb 88 (manuscript received 20 Nov 86) pp 54-57

[Article by A. V. Sanin, T. A. Krasnyanskaya, Ye. B. Mysyakin, N. G. Sinilova, A. P. Duplishcheva, and M. A. Tumanyan, Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Ongoing testing was continued on the bioactivities of the bacterial polysaccharide derived from Salmonella abdominalis, designated salmosan, to assess the effects on the hemopietic system of CBA and (CBA x C57Bl/g)F_1 mice. Intraperitoneal administration of salmosan in doses of 1, 10, or 100 μg to sublethally irradiated (5.5 Gy) mice stimulated dose-dependent proliferation of hemopoietic stem cells when assessed in terms of CFUs. Maximum effect was obtained when salmosan was administered 24 h before irradiation irradiation, with recovery of hemopoiesis evident in the spleen, bone marrow, and blood within 1 to 9 days. In the case of bone marrow, the pool of CFUs a day after salmosan administration in a dose of 1, 10, or 100 μg was, respectively, 13.1, 41.2, and 76.6 percent. Furthermore, studies with irradiated hybrid recipients and salmosan-treated donor mice led to the demonstration that the latter formed thymic cells capable of suppressing the graft-versus-host response in the former animals. The appearance of the suppressor cells became evident 2 weeks after treatment with salmosan, displaying again dose-dependent characteristics. Figures 3; references 21: 6 Russian, 15 Western.

UDC 612.017.1.014.46:615.276.4

Bacterial Polysaccharide Salmosan Enhancement of Resistance to Infection

18400029d Moscow IMMUNOLOGIYA in Russian No 1, Jan-Feb 88 (manuscript received 12 Jun 86) pp 60-62

[Article by A. P. Duplishcheva, Ye. B. Mysyakin, Ye. I. Romashevskaya, N. G. Sinilova, and M. A. Tumanyan,

Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Salmosan, a polysaccharide isolated from Salmonella typhi$_2$ 4446, was tested in outbred and C57B1 and (CBA x C57B1/6)F$_1$ male mice for its effects on resistance to infection. The animals were treated intraperitoneally with 100 μg salmosan 1-7 days before intraperitoneal infection with either S. typhi$_2$ 4446 or Klebsiella pneumoniae in LD$_{50}$ doses. In all cases salmosan increased the resistance of the animals 10- to 40-fold, with best results obtained with salmosan administered 1 day before infection. Salmosan also activated peritoneal macrophages as evident by depression of 5'-nucleotidase activity, an effect that persisted for 28 days and was evident within 1 day of salmosan administration. In addition, salmosan also stimulated spontaneous antibody formation against SRBC in the spleens of treated mice, indicating activation of B cells. The data thus pointed to the fact that salmosan exerted multifaceted effects on the immune system culminating in enhanced resistance to infection in mice. Figures 2; references 11: 5 Russian, 6 Western.

UDC 615.371:578.832.1].012.6

Efficacy of Immunization with Liposome-Enclosed Surface Antigens of Influenza Virus by Various Routes

18400033a Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 2, Mar-Apr 88 (manuscript received 26 Nov 86) pp 151-153

[Article by S. A. Burkhanov, L. A. Mazhul, V. P. Torchilin, O. N. Ageyeva, T. S. Saatov, and O. G. Andzhaparadze, Moscow Scientific Research Institute of Viral Preparations, USSR Ministry of Health; VKNTs [not further identified], USSR Academy of Medical Sciences, Moscow]

[Abstract] Comparative immunization trials were conducted to assess the efficacy of liposome-enclosed surface antigens of influenza virus vis-a-vis the soluble antigens and whole virus vaccine. Influenza A/PR8/34 neuraminidase and hemagglutinin were incorporated into liposomes prepared from lecithin and cholesterol (10:4), and used for intraperitoneal and intranasal administration to BALB/c mice 2 weeks prior to challenge with the live virus (intranasally, 2 LD$_{50}$ dose). The survival figures for the liposome vaccine were dose-related: 77 percent with 5 μg antigen protein per mouse, and 100 percent with 20 μg/mouse. The survival rate for control (unimmunized) mice was 5 percent. Maximum survival rate with 20 μg/mouse of the soluble antigens was 66 percent, and with the whole virus vaccine 100 percent (50 μg/mouse). On intravenous administration, the liposomal vaccine was relatively ineffective. These observations indicate that liposomally enclosed influenza antigens constitute an effective dosage form in the management of murine influenza and suggest the use of this approach to the creation of more effective influenza vaccines. Figures 2; tables 1; references 7: 3 Russian, 4 Western.

UDC 615.371:578.821.51+378.891].015.4:612.017.1].07

Human and Rabbit Antibody Response Against Vaccinia Virus Following Immunization with Recombinant Vaccinia-Hepatitis B Vaccine

18400033b Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 2, Mar-Apr 88 (manuscript received 06 Mar 87) pp 175-179

[Article by N. V. Chelyapov, V. I. Chernos, and O. G. Andzhaparidze, Moscow Scientific Research Institute of Viral Preparations, USSR Ministry of Health]

[Abstract] An immunoblotting study was conducted with human volunteers and rabbits to assess the effects of the incorporation of foreign genetic material into the vaccinia virus on the immune response. The study was based on the fact that the vaccinia virus appears to be one of the more promising candidates for genetically engineered vaccines. The immunizations were carried out with the LIVP strain of vaccinia virus and its genetically engineered congener bearing the S gene for the hepatitis B surface antigen (LIOGEN-HB/C2-TK$^-$) and the herpes simplex TK gene (LIOGEN-HB/C2-TK$^+$). Analysis of the sera of volunteers immunized 10-15 years ago with vaccinia showed the presence of antibodies against nucleoid proteins 135K, 88K, 60K, and 26K, as well as against surface proteins 42K, 35K, and 11K. One month after vaccination with the recombinant vaccine the levels of these antibodies showed an increase, while the antibody spectrum remained unaltered. Furthermore, there was no correlation between the degree of stimulation and the TK pheno-type of the recombinant virus. Rabbits immunized with the recombinant virus presented with antibodies directed against 135K, 88K, 62K, 60K, 42K, 35K, 30K, 26K, 23K, 21K, 15.5K, and 11K proteins. The fact that the immune response in both cases encompassed high levels of antibodies against internal viral antigens was surprising. This fact may indicate that the production of such antibodies and their long-term persistence is related to some, as yet undefined, immune role of these antigens, perhaps in cellular immunity, since it has previously been assumed that immunity is primarily due to the superficial viral antigens. Figures 2; references 11: 4 Russian, 7 Western.

UDC 615.37:578.245].076.7

Effects of Recombinant Interferon (Reaferon) on Human Cell Continuous Culture

18400033f Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 2, Mar-Apr 88 (manuscript received 14 Jul 86) pp 247-250

[Article by A. M. Amchenkova, A. N. Narovlyanskiy, L. N. Pokidysheva, F. V. Voronina, and Ya. Ye. Khesin, Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Soviet recombinant interferon, series R-3 reaferon, produced in a B. pseudomonas sp.VG84 system,-

was tested for its mitotic effects on a human cell continuous culture. Prior studies with human leukocyte interferon showed inhibition of mitotic activity of the cell culture in question (line J-96) by 45-71 percent in the case of native cells, and by 15-50 percent in the case of purified cells, depending on the time of application. Addition of reaferon to a 24 h J-96 culture yielded a 21.7 percent inhibition with 100 U/ml of reaferon, and 27.8 percent inhibition with 1000 U/ml. However, addition of reaferon at 96 h elicited a paradoxic response in that the mitotic activity increased by 50-100 percent in a dose-dependent fashion 1 day after addition. Furthermore, addition of reaferon to 48 h J-96 cultures uniformly enhanced mitotic activity by 26 to 40 percent. These observations demonstrated significant differences between natural and recombinant interferons. It is particularly noteworthy that once the monolayer is formed, reaferon enhances mitosis and to some extent prolongs the viability of aging cells in the test system utilizing J-96 cells. References 16: 7 Russian, 9 Western.

UDC 615.849.19.035.2:621.375.826.039.58

Establishing Standards for the Safe Use of Laser Units in Treatment Facilities

18400021b Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 4, Apr 88, pp 17-19

[Article by Col. V. M. Gavryutin, Lt. Col. Ye. G. Zhilyayev, and Lt. Col. N. S. Kopovoy, Medical Service]

[Abstract] Medical lasers are categorized according to the level of hazard they represent in the workplace. The emissions of category 1 lasers are not considered dangerous, while those of category 2 can damage the eye if it is struck by a direct or specularly reflected beam. Category 3 lasers comprise those that can damage the eye with a direct or specularly reflected beam or with diffusely reflected radiation when the eye is 10 cm or less from the reflecting surface. The skin can also be injured with direct or specularly reflected radiation of category 3 lasers. Category 4 represents lasers whose emissions—direct, specularly reflected, and diffusely reflected at 10 cm or less—represent a danger to both eye and skin. Most medical lasers fall in categories 3 and 4. A number of measures have been taken to ensure the safety of those who operate or are treated by lasers. Specifically, lasers must be assembled and checked at the treatment facility by the manufacturer, who also establishes the tuning protocol. Location requirements for each category and type of laser unit are spelled out in the SNiP II-69-78 regulations, and department heads are responsible for the safe operation of the lasers .

UDC 617.713-018.73-018.15-02:615.849.19

Mitosis in Rabbit Corneal Epithelium in the Norm and After Local Irradiation of Various Skin Areas by Infrared Laser

18400034c Moscow PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA in Russian No 2, Mar-Apr 88 (manuscript received 21 Jul 86) pp 81-84

[Article by A. V. Denisov, V. A. Kashuba and R. A. Druzhinina, Moscow Medical Institute of Stomatology imeni N. A. Semashko]

[Abstract] The skin of various parts of the body of experimental animals was exposed to a single pulse of a powerful IR laser beam to determine indirect (long-term) effects on mitosis. Mitosis was selected as the criterion of photobiologic effect on the body because it is an integral indicator of the condition of the cell proliferation regulation system. The testing site was the corneal epithelium, which is quite sensitive to extremal factors. An equation was derived to describe the normal diurnal variation of proliferation intensity in the rabbit corneal epithelium. Local irradiation of various areas of the body was found to cause variation in this characteristic in both directions. The maximum rate of proliferation of 4-6‰ was observed between 10 am and 1 pm. The total number of pathological mitoses in the irradiated animals was 3-4 times greater than the mutations in the corneal epithelium cells of the controls, indicating damage to the system that regulates proliferation and protects the genetic apparatus from mutation and suggesting that IR laser radiation can adversely affect cell division in body. Figure 1, references 7 (Russian).

UDC 615.832.12-03:617

Hyperbaric Oxygenation in Modern Surgery

18400022a Moscow KHIRURGIYA in Russian No 6, Jun 88 (manuscript received 18 Jan 88) pp 141-146

[Article by S. N. Yefuni, All-Union Scientific Center of Surgery (Director: B. V. Petrovskiy), Moscow]

[Abstract] General and regional hypoxia along with endogenous intoxication forms the pathophysiological basis for all critical states regardless of their etiology. Therefore, an active search is underway for measures aimed at increasing the body's tolerance to oxygen deficiency. Hyperbaric oxidation (HBO) is highly effective in prevention and treatment of many serious pathological states. HBO coupled with hyperthermia is often used in reconstructive cardiosurgical interventions in which the heart needs to be isolated from blood circulation. In recent years, this approach was extended to reconstructions of major arteries, to surgery of respiratory organs, gastrointestinal tract, urological and obstetrical operations and other high risk operations. A separate application of HBO is in the treatment of wound infections due to anerobic and clost-ridial microflora and facultative spore non-producing anerobes. This method lowered mortality, shortened hospital stay, diminished the number of amputations and economized on expensive medications. A number of these HBO effects such as detoxifying, immunomodulating, cardioprotective effects are due to "pharmacologic" effect of hyperoxia on the structure and metabolism of the cells of involved organs. In spite of some still unanswered questions (such as optimal regimens, individual prognoses) this method grows in popularity. Presently there are 500 active HBO centers in the USSR. References 13: 7 Russian, 6 Western.

UDC 616.12-073.97:681.11.034.7

Optimization of Parameters of Remote Transmission System of Frequency Modulated EKG Signals

18400022b Moscow MEDITSINSKAYA TEKHNIKA in Russian No 2, Mar-Apr 88 (manuscript received 21 May 87) pp 32-39

[Article by V. M. Koltun and Yu. S. Trusov]

[Abstract] Remote transmission of EKG signals became a popular diagnostic technique in the middle 60's. Dozens of remote-consultative centers were organized on its basis. Three types of instruments are produced domestically for this purpose: "Svyaz," "Volna-1," and "SPEKS-T-ol." All of them, as well as the foreign models, are based on analog frequency modulation (FM) carrying tonal signal frequencies. In recent years, digital transmission systems were developed for this purpose showing much lower error rate, but they are bulky and expensive. Both systems will probably supplement each other in the future rather than replace one. Therefore, this work was devoted to optimization of principal parameters of the analog-based system. A mathematical model was developed for fluctuating errors in telephone lines. Based on theoretical and experimental analysis, optimal parameters were found for telephone transmitters and receivers of EKG signals: f_o=1700 Hz; m=3.3; f=330 Hz; F=1030 Hz (with section frequencies f_H=1185 and f_B=2215 Hz). Figures 2; references: 4 (Russian).

UDC 616-005.1-036.11-085.384-092.9-07:616.151.5-07

Status of Blood Coagulation System in Dogs Following Acute Hemorrhage and Replacement Therapy with Polyglucin and Perfluorocompound Emulsion

18400035c Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 5, May 88 (manuscript received 16 Feb 87) pp 29-31

[Article by S. M. Panchenko and N. I. Afonin, doctor of medical sciences, Central Scientific Research Institute of Hematology and Blood Transfusion, USSR Ministry of Health, Moscow]

[Abstract] The status of blood coagulation was studied in a model system employing 8-12-kg outbred dogs subjected to acute hemorrhage (50 ml/kg) and treated with polyglucin transfusion (35 ml/kg) followed by perfluorocarbon emulsion (24 ml/dL) in a dose of 25 ml/kg. Control animals were treated with polyglucin (35 ml/kg) and physiologic saline (25 ml/kg). Thromboelastographic studies were commenced 24 h later and continued for 42 days, and complemented by other studies designed to yield a comprehensive picture of the coagulation system. In the case of both forms of therapy marked alterations in coagulation were evident. However, in the control animals treated with polyglucin and physiological saline, recovery of normal coagulation was apparent in 14 to 21 days. In the case of dogs treated with polyglucin and the perfluorocarbon emulsion, selected parameters such as the prothrombin index, total fibrinolytic activity, and plasma fibrinogen activator failed to return to baseline levels by day 42. In summary, therapy with polyglucin and the perfluorocarbon emulsion had a more profound effect on the coagulation system. Within 1 day of treatment the control dogs presented with depressed thromboplastin synthesis, prolongation of recalcification time, and more pronounced reduction in thrombocyte counts than the animals treated with the perfluorocarbon chemicals. The experimental animals showed recovery within the first 7 days, and between day 7 and 21 presented with exacerbated procoagulant activity. Figures 4; references 11: 5 Russian, 6 Western.

UDC 615.384:547.963.4].012.1.011.4

Physicochemical and Biological Properties of Chemically Modified Bovine Globin

18400035d Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 5, May 88 (manuscript received 11 Feb 87) pp 32-34

[Article by M. V. Gudzhabidze, T. V. Tkeshelashvili, and G. Ya. Rozenberg, professors, V. M. Shlimak and K. N. Gachechiladze, doctors of medical sciences, and E. V. Shtykova, Scientific Research Institute of Hematology and Blood Transfusion, imeni Acad. G. M. Mukhadze, Georgian SSR Ministry of Health, Tbilisi; Central Scientific Research Institute of Hematology and Blood Transfusion, USSR Ministry of Health, Moscow]

[Abstract] Formaldehyde-crosslinked bovine globin molecules were evaluated for their physicochemical and biological characteristics with a view toward use of them as potential blood substituents. For biological testing a 6 percent preparation was utilized and shown to have an average MW of 150,000 to 200,000 D, a colloidal osmotic pressure of 2. to 2.5 kPa, an osmolarity of 280-290 mosm/liter, and a relative viscosity of 2.2 to 2.4. Immunization of rabbits with the 6 percent globin solution in Freund's complete adjuvant failed to elicit antibodies under conditions that elicited an immune response against human and bovine hemoglobin. In addition, the globin preparation was nontoxic in mice and did not elicit an anaphylactic response in guinea pigs. Studies on dogs subjected to massive hemorrhage (45 ml/kg) demonstrated its efficacy in maintaining blood pressure at 142 mmHg for 4 h (158 mmHg control value) and a circulating blood volume of 100 ml/kg, with survival of the animals on subsequent days of observation following the blood loss. These studies demonstrated that formaldehyde-crosslinked bovine globin preparation was relatively areactogenic, nonantigenic, and effective in preliminary experimental studies in correcting hemodynamic perturbations resulting from extensive blood loss. Figures 1; references 8: 4 Russian, 4 Western.

UDC 617-001.17-06-085.373.6-039.71

Prevention of Infectious Complications in Burn Patients with Immunoglobulin Preparation Containing Normal Antitissue Antibodies

18400035e Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 5, May 88 (manuscript received 14 Apr 86) pp 38-41

[Article by R. I. Murazyan (deceased), N. R. Panchenkov, N. S. Murashova, and M. A. Kozlova, Central Scientific Research Institute of Hematology and Blood Transfusion, USSR Ministry of Health, Moscow]

[Abstract] Therapeutic trials were conducted on 8 patients with 2d to 4th degree burns to assess management with an immunoglobulin preparation containing normal antitissue antibodies. The immunoglobulin preparation was derived from plasma donors that had been immunized by combined administration of autologous blood and prodigiosan. The resultant immunoglobulin preparation consisted of a 5 percent protein solution that was nontoxic, apyrogenic, and heat stable. The patients were treated with 3-4 ml of the preparation on alternate days for a total of 4-5 treatment beginning with the 2d to 10th day of trauma. None of the patients developed infectious complications despite extensive and deep burns as a result of the immunotherapy applied in conjunction with conventional therapeutic modalities. The clinical course in 8 patients was favorable and, following a full course of immunotherapy, contamination of the wounds was reduced 10^2- to 10^5-fold. Healing occurred at a faster pace with the patients undergoing skin grafting with 100 percent success in 18-27 days. Evaluation of the immune status of the patients demonstrated that treatment with the immunoglobulin preparation resulted in a more than 2-fold increase in T cells, enhanced phagocytic activity, and—in most of the patients—increased serum levels of interferon, lysozyme, and beta-lysins. Administration of the immunoglobulin preparation was not complicated by any local or systemic side effects. One patient succumbed as a result of system failure but without any infectious complications. These observations suggest that immunoglobulin preparations with normal antitissue antibodies should be considered for more extensive application in the treatment of burn patients. References 9 (Russian).

UDC 616-006-033.2-08:615.277.3muramyl dipeptide]-092.9

Antimetastatic Efficacy of Liposome-Enclosed Muryl Dipeptide Analog

18400037c Leningrad VOPROSY ONKOLOGII in Russian Vol 34 No 4, Apr 88 (manuscript received 8 Apr 87) pp 433-438

[Article by V. Yu. Umanskiy, A. V. Stefanov, O. P. Bondar, K. P. Balitskiy, V. G. Pinchuk, and V. K. Lishko, Institutes of Oncologic Problems imeni R. Ye. Kavetskiy and of Biochemistry imeni A. V. Palladin, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] Experimental therapeutic trials were conducted with N-acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMAI) in C57B1 mice to determine its efficacy in controlling metastases. The therapeutic model consisted of mice injected into footpads with 2 x 10^5 Lewis lung carcinoma 3LL cells, followed by amputation of the extremity at the knee joint 14 days later for removal of primary tumor. Therapy consisted of intravenous administration of liposome-encapsulated GMAI calculated to give a 62.5 μg/kg dose per injection. In untreated animals amputation resulted in a 2.1-fold increase in the bulk of pulmonary metastases and in a 1.4-fold increase in the number of

metastases in comparison with mice without the amputation. Mice treated with 4 injections of GMAI, commencing 4 days after the amputation, showed a reduction in both the bulk and number of pulmonary metastases (7.5- and 2.4-fold, respectively). Optimum benefit, however, was obtained when GMAI was administered 8 times before and after the amputation, beginning 4 days after implantation of the malignant cells. In the latter case the number of pulmonary metastases decreased 3.8-fold and their bulk showed a 14-fold reduction. A second course of 8 injections, commencing 27 days after the operation, yielded a 150 day survival figure of 56 percent. In the untreated control group there were no survivors after 40 days. Evaluation of adenosine metabolism in alveolar and splenic macrophages demonstrated that tumor progression was accompanied by physiological deterioration of the macrophages, whereas GMAI promoted physiological recovery of the cells. On balance, the observations demonstrated that GMAI was effective in controlling pulmonary metastases when administered as a liposomal preparation, a dosage form favoring localization in macrophage-rich organs. References 15: 9 Russian, 6 Western.

UDC 57.082.56

Storage of Microbial Inoculation Cultures at Low Temperatures

18400027 Moscow MIKROBIOLOGIYA in Russian Vol 57 No 2, Mar-Apr 88 (manuscript received 7 Aug 86) pp 333-337

[Article by S. S. Avtushenko, Ye. I. Babkin, O. G. Aleksandrenkova, V. A. Balmasov, V. I. Batarin, and T. G. Yaremenko, All-Union Scientific Research Institute of Especially Pure Biopreparations, Leningrad]

[Abstract] The search for new, more effective methods to preserve microorganisms has reached new intensity levels in recent years. One of the more promising methods utilizes ultralow freezing of the microorganisms. The goal of this work was to investigate the potential of cryopreservation of inoculation cultures. Escherichia coli M-17 and Serratia marcenscens B-10 M-1 bacteria were deep-frozen to -196 degrees C, stored for periods of up to 1 year and recultivated. It was shown that the material stored at -196 degrees C gave the same yield of the biomass as fresh inoculation material. The process was reproducible and standardized with respect to the biomass and the products of microbial synthesis. Cultures grown from the low temperature material were resistant to freeze-thawing to the same extent as their parent cultures. References 15: 6 Russian, 9 Western.

UDC 576.8

Biological Activity of Parasporal Crystals in Bacillus Thuringiensis

18400069b Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 3, May-Jun 88 pp 427-436

[Article by T. G. Yudina, N. S. Yegorov, Zh. K. Loriya and S. N. Vybornykh, Biology Faculty, Moscow State University]

[Abstract] A literature survey was conducted on the spectrum of biological activity and putative origin(s) of the parasporal crystal protein of several subspecies of Bacillus thuringiensis. Evaluation of the data on biological activities of this protein (delta-endotoxin) include antibiotic potential against a variety of Gram positive organisms, as well as the better recognized entomocidal potential. On these grounds, the delta-endotoxin combines the characteristics of an insecting along with those of a bacteriocin. The evolution of the genome segment responsible for delta-endotoxin appears to be, at the very least, dual in nature. The indication is strong that insecticidal and antibacterial activities may be due to DNA sequences having their origins in insect viruses and bacteriophages, respectively, while expression of innately bacterial DNA segments is responsible for the inherently toxic features of the delta-endotoxin molecule. References 66: 21 Russian, 45 Western.

UDC 351.86:356.33:355.332:355.257.6

Role of Sanatorium Selection Committees in Mass Health Screening System

18400021a Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 4, Apr 88, pp 15-1

[Article by Col. O. I. Gorshkolepov, Medical Service]

[Abstract] Continuity of examination and treatment of patients requiring sanatorium and resort treatment is suffering because mass screening data are not being used properly by the committees responsible for sending patients for treatment and because the regulations established for the sanatorium selection are not being strictly followed. Selection committee members often limit their activities to mere authorization of sanatorium passes, although their responsibilities include a much wider range of duties, including acting as a consultant to the treating physician when the determination is being made on whether a patient needs sanatorium care, what type of sanatorium the patient needs, and the best time to send the patient for treatment. Committee members must be well-versed in sanatorium treatment and in the symptomatology of various diseases and must work closely with clinical committees. Selection committee members must see to it that patients dispatched to sanatoria have the proper medical documentation and that they are issued sanatorium passes early enough to be able to report on time. The selection committee is also responsible for continuity of post-sanatorium care and the issuance of post-sanatorium reports and analyses.

UDC 579.25.5

Regulation of Escherichia Coli htpR Gene Expression by Means of Antisense RNA

18400023a Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 22 No 2, Mar-Apr 88 (manuscript received 2 Jun 87) pp 454-458

[Article by V. I. Kiselev and I. M. Tarasova, Institute of Applied Molecular Biology, USSR Ministry of Health, Moscow]

[Abstract] In recent years, effective methods have been developed for superproduction of heterologous proteins in bacterial cells. However, synthesis of eukaryotic proteins met with difficulties related to proteolytic split of the protein. To some extent this problem could be solved by using as recipients E. coli mutants defective in proteolytic degradation of heterologous proteins. In the present work, a method is proposed based on the plasmid pCQV2 containing thermoinductive regulatory elements of bacteriophage λ for the synthesis of a new vector which makes it possible to combine inducible synthesis of foreign proteins with negative control of intracellular proteolysis. The principle of gene expression regulation by antisense RNA was used. Gene htpR fragment coding N-terminal polypeptide portion was cloned in reverse orientation in the restrictase Sal 1 recognition fragment of the plasmid pCQV2. At 42 degrees C a transcription with P_r-plasmid promotor was initiated leading to the synthesis of antisense RNA of the hrpR gene, which regulates transcription of three genes coding proteases lon, groES and groEL. Under conditions of P_r transcription, the induction of bacterial growth carrying recombinant plasmid was delayed and degradation of puromycin polypeptide was decreased 3-fold. Figures 2; references 17: 1 Russian, 16 Western.

UDC 576.8.097.29

Comparison of pH and Temperature Effects on Conformations of Binding Subunits of Plant Toxins Ricin and Omela 1 Lectin

18400023b Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 22 No 2, Mar-Apr 88 (manuscript received 16 Jun 87) pp 493-497

[Article by T. L. Bushuyeva, A. G. Tonevitskiy, and N. A. Maysuryan, All-Union Cardiologic Scientific Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] Plant toxins ricin, from castor oil plant, and lectin, from omela 1, have similar structures and functions. They consist of two polypeptide chains with almost the same 30kD molecular weight, connected by a disulfide bond. In the present work, attention is given to changes taking place in the B-subunit during transition from neutral to acid (4-5) pH and compared to structural alterations due to heat denaturation (45 degrees C) and the results of a treatment with guanidine dihydrochloride (3M). It is shown that, at low pH and high temperature, protein conformations are similar but not identical—differing from the native conformation by low fluorescence intensity and by the fact that tryptophan radicals are more accessible to the solvent. Also, they differ from the completely unfolded conformation resulting from treatment with guanidine dihydrochloride. An assumption is expressed that partially denatured B-chain protein is an intermediate state of the toxin obtained during interaction with cell membrane. Figures 6; references 18: 5 Russian, 13 Western (2 by Russian authors).

UDC 577.1

Specific Reception of ds-RNA on Plasma Cell Membrane

18400025 Yerevan DOKLADY AKADEMII NAUK ARMYANSKOY SSR in Russian Vol 86 No 4, 1988 pp 174-177

[Article by R. A. Zakharyan, K. A. Bakunts, and N. A. Skobeleva, Institute of Experimental Biology, ArSSR Academy of Sciences]

[Abstract] Di-spiral RNA (ds-RNA) act as inducers of interferon, stimulators of primary and secondary immune responses and modulators of biochemical reactions. ds-RNA was shown to adhere to plasma membrane of nerve cells, liver cells, and bone marrow, penetrate the membrane barrier and enter the cell itself. Specific interaction process of ds-RNA with surface membrane and isolated plasma membrane of nerve cells was studied. Cell surface in suspension obtained immediately after trypsin dissociation of nerve tissue was unable to accept ds-RNA molecules. This ability was recovered after 4 days of cultivation. Another trypsin treatment removed completely the ability to bind ds-RNA. Treatment of cells with DNA-ase or RNA-ase had no effect on the ds-RNA absorption on the cell membrane. The reaction of ds-RNA with plasma membrane of brain cell proteins appeared to be highly specific, resembling ligand-receptor interaction. In presence of ds-RNA, absorption of mouse encephalomyocarditis virus on plasma cell membrane is inhibited, 75-80 percent, due to the blocking of the receptor, its chemical modification and a change in lipid surroundings around the receptor. Figures 2.

UDC 579.842.11.254

Construction and Stability of Vectors for Expression of Heterologous Genes Under Control of Highly Efficient E. Coli and Coliphage Promoters

18400059a Moscow BIOTEKHNOLOGIYA in Russian Vol 4 No 3, May-Jun 88 (manuscript received 30 Jan 87) pp 325-334

[Article by M. E. Trukhan, A. V. Mochulskiy, M. I. Lebedeva, A. L. Lapidus, S. M. Podkovyrov and S. V. Mashko, All-Union Scientific Research Institute of the Genetics and Selection of Industrial Microorganisms, Moscow]

[Abstract] A novel vector molecule, plasmid pML24, has been constructed for the selective cloning in E. Coli

systems of highly efficient promoters. pML24 has been derived from pML4, a plasmid that ensures efficient expression of the cat gene following integration of foreign promoter sequences. As a result, a series of recombinant plasmids have been constructed that contain the promoters trp OP, tac, P_L, or P_R before the cat gene and differ by the presence or absence of ρ-independent transcription terminator sequences. The stability of the resultant plasmids in E. coli strains was assessed under conditions of cloned promoter derepression, demonstrating a positive correlation between the efficiency of a promoter and the rate of loss of plasmids lacking transcription terminators. Transcription of the cat gene with P_L promoter in a system containing an intact nut L locus and an active bacteriophage lambda N gene is not terminated at the ρ-independent terminator tandem and, accordingly, the corresponding plasmids are lost as rapidly as plasmids lacking terminators. The occurrence of terminator-like sequences in secondary mRNA structure in cases of inefficient cat translation may stabilize plasmids with trp promoter even in the absence of additional ρ-independent terminators. The introduction of ρ-independent terminators into the 3'-end of the cat gene ensures plasmid stability for at least 6-10 h after promoter derepression. This phenomenon facilitates the use of such recombinant plasmids as vectors for highly-efficient expression of heterologous genes in E. coli. Figures 6; references 17: 5 Russian , 12 Western.

UDC 577.15

Structure of Binding Center of Gaba Receptor
18400069c Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 3, May-Jun 88 (manuscript received 27 Feb 84) pp 478-480

[Article by M. M. Kats, Scientific Research Institute for the Biological Testing of Chemical Compounds, Kupavna]

[Abstract] Studies were conducted on the binding of radio labeled GABA and various GABA congeners to GABA receptors to assess the nature of the binding center. Corey-Pauling-Koltun atomic models were used to model the disposition and orientation of functional groups at the binding center on the basis of binding affinities. The resultant data indicated that the actual binding center within the GABA receptor encompasses an anionic site and a cationic fragment represented by guanidine (suggesting the involvement of arginine). Graphic presentation is made of the relative locations of the anionic and the cationic moieties, noting that analyses of this kind facilitate studies on the search for GABA agonists and antagonists. Figures 1; references 6: 2 Russian, 4 Western.

Regulatory Peptides of Strong and Rapid Action

18400051 Moscow PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA in Russian No 3, May-Jun 88 pp 3-8

[Article by I. P. Ashmarin]

[Text] In spite of the abundance of published material on regulatory peptides (RPs) indicating the extremely wide range of their biological activity, the notion persists that RPs are comparatively "soft" modulators of physiological functions that rarely yield rapid, pronounced effects. Two circumstances serve as the source of such a notion. First, when this field of study was coming about (in the late 1970s), attracting particular attention were natural RPs that were rapidly split by proteases in the internal media of the body (enkephalins, for example, and ACTH 4-7-10) and had an effect that could be detected only in certain experimental conditions (delta-sleep peptide, for example). Second, the rather broad-based experience garnered in earlier decades in the study of large RPs—protein hormones (insulin and somatotropin, for example)—and small peptide hormones (vasopressin, oxytocin, and thyroliberin [TRH]) was viewed as a somewhat isolated group of data. The fact that these compounds were traditionally placed in the category of hormones had a psychological effect, whereas it was hard to classify many of the RPs discovered in the second half of the 1970s as hormones. Back then, vasopressin, oxytocin, bradykinin, and angiotensin II could already be categorized as strong, rapidly acting small RPs. But even with that, the extraordinary lability of the last two RPs left an impression: their half-life in the body was 15-100 seconds. Finally, nothing was known of a unique phenomenon—the prolonged action of certain short-lived RPs, probably mediated by trigger or cascade regulatory and metabolic processes.[7,15,24,34]

At present, many small and medium-sized RPs that have a strong and rapidly acting effect on the body with systemic administration have been discovered and studied to varying degrees. Effects exhibited in systemic administration attract special attention because strong central effects are inherent, to some extent, to a great many RPs. Naturally, powerful peripheral action is seen primarily in RPs developed and secreted outside the blood-brain barrier. There are now known to exist, however, a number of RPs whose action in systemic administration is determined to a varying degree when they overcome the blood-brain barrier and interact with receptors located in the central nervous system. It is also important to emphasize that in a number of cases, the absence of information on the strong and rapidly acting effects of RPs was due to the fact that the conditions for their appearance, which, as it turns out, were often associated with pathology, were not known. We will examine further these RPs, limiting their characteristics to the physiological effects that arise in systemic administration and that last at least an hour or so.

Thyroliberin (TRH). The manifold effect of TRH in systemic administration attracted attention as far back as the early 1970s. Here, however, we will not only depict its effects in greater detail, but also identify new TRH effects.

TRH affects respiratory activity, especially in depressed breathing, in certain forms of shock and in a number of spinal disorders. It is also possible that in the near future, TRH's ability to relieve certain forms of reactive mental depression will be included in the list of its strong and rapidly acting effects. As can be seen, the entire list is associated with pathology. Classical liberin effects are placed in the category of strong, rapidly acting, but not quite as impressive, effects: stimulation of the excretion of thyrotropin and prolactin, used for diagnostic purposes.

That TRH intensifies respiratory activity was established on various experimental animals—such as frogs, rats, cats, and monkeys.[8,12,29,30,38] The target of action is apparently the respiratory center or the structures directly connected to it, which suggests the partial penetration of systemically administered TRH through the blood-brain barrier.[4,5,8,12] Attracting the most attention at this time is the restoration of breathing and hemodynamics disrupted by such things as hyperventilation the effects of opiates, blood loss, and a severed vagus nerve.[4,5,8,11,14] The duration of the effect of TRH in one-time systemic administration (in doses of 5-50 μg/mg) is measured in hours. Since the clinical use of one-time administration of TRH for diagnostic purposes was allowed universally in those same doses even before the experiments, it is advisable that injectable TRH preparations be at the immediate disposal of physicians, if only in the leading clinics. The inherent dangers associated with the stimulating effect TRH has on the thyrotropin system—T_3 and T_4—should not, as a rule, be considered a contraindication for one-time use. In emphasizing this circumstance, we are by no means casting doubt on the expansive research conducted on the creation of TRH analogs that are not capable of inducing thryotropin, but do preserve other useful properties.[13,16,17,37] Many such analogs, including domestically produced analogs,[17,37] are already undergoing clinical tests. At this point, however, it is advisable to use the treatment potential of the best-studied preparation of natural TRH.

Closely related to the above-described effects of TRH and its analogs is the preparation's favorable effect not only on disturbed respiratory activity, but also on other mainfestations of shock states caused by intoxications and blood loss. At present, that means of treating shock is well-studied by a group of American researchers[30,31] who, with various routes of administration of TRH and its analogs, showed that the effectiveness of such preparations against shock is comparable to that of naloxone. One element of this effect may be the indirect antagonism of TRH with opioid peptides, whose level grows sharply in shock, as well the ACTH excretion partially stimulated by TRH, the antishock activity of which is examined in the next section.

The coexistence and "collaboration" between TRH and such neuromediators as serotonin and substance P in many neurons of spinal cord and the medulla oblongata are apparently the basis for the favorable effects of TRH in various spinal disorders, including ataxia of varying origin and a number of spastic states.[44,48] TRH's activity in this regard correlates with a reduction in its level in the spinal fluid in such states.

The literature includes data on the antidepressant effects of TRH.[25,28,49] There is reason to believe that the realm of practical application of TRH may be confined to specific forms of reactive mental depression[1] as opposed to endogenous depressions, in which TRH effects are variable or are limited in duration. Again, attracting attention is the effectiveness of one-time administration of TRH in doses of up to 10 μg/kg. Also interesting is information on the "dramatic" effect of a combination of TRH and small doses of neuroleptics on the state of depressed indivduals.[25]

Accordingly, based on the pronounced nature of the effects of TRH in the many pathological states enumerated above, on its dose level, and on the speed of onset of its action, TRH obviously belongs in the group of RPs that are the focus of this survey.

ACTH and its fragments. The long established and thoroughly studied function of ACTH is the stimulation of corticoid production. In experiments with healthy animals, this effect is manifested in systemic administration at doses on the order of 10-100 μg/kg and is accompanied by pronounced and rapid external manifestations. Systemic administration of the fragments $ACTH_{4-7}$ and $ACTH_{4-10}$exerts an influence on such functions as learning capacity and attention. It is also difficult to label these effects as strong and rapid. Intravenous injection of $ACTH_{1-24}$ in doses of 80-160 μg/kg in healthy animals has no appreciable effect on the cardiovascular or respiratory system. In addition, it has long been known that ACTH release is associated with intense processes, such as stress and shock. It is not surprising, then, that the strong and rapid effects of the large $ACTH_{1-24}$ fragment show up in research involving the correction of disturbances of hemodynamics and breathing after extensive blood loss (following hemorrhagic shock).[21] The researchers call the $ACTH_{1-24}$ effects they observed "dramatic." In fact, the blood losses were so great in those experiments that virtually all the animals in the control group, who received a normal saline, died. To a large extent, the intravenous injection of of 100-160 μg/kg $ACTH_{1-24}$ normalizes (in 15-30 minutes) arterial pressure and breathing, successfully averting death in the animals. This effect of $ACTH_{1-24}$ is reduced against the background of morphine administration and, similar to the action of TRH described above, may be associated with antagonism in relation to endogenous opioids.[14] And in this case, it must be emphasized that the presence of a pathology is a necessary condition for the manifestation of a pronounced effect by the preparation.

Unlike TRH, additional experimental research should probably precede the use of this effect of $ACTH_{1-24}$ in the clinic. Until now, rats and dogs have been the subjects of the research.

Somatostatin. The classical object of the action of somatostatin is the productionof growth hormones, which, in the final analysis, presumes long-term if, possibly, strong effects. For that reason, the identification of rapidly acting and strong effects of this RP is an example of psychologically difficult to discern facts. We have in mind the suppressive effect somatostatin has on gastrointestinal hemorrhage—an effect well documented in a number of studies.[6,36] Here also, the strong and rapid action is coupled to pathology. Although there is not yet any basis for putting other nonhormonal effects of somatostatin (on functions such as carbohydrate metabolism, temperature regulation,and tumor growth) in the category of rapid and strong effects, their importance is beyond question.

Co-calcigenin. In the foreign literature, this RP is called calcitonin gene-related peptide (CGRP), i.e., a peptide related to the gene that codes calcitonin. Both expanded forms of the name are extremely inconvenient. So is the abbreviation CGRP, since, unlike in a number of other instances, supplying an equivalent Russian abbreviation is difficult. For that reason, the commonplace name that is becoming popular—co-calcigenin—will be used henceforth.

Co-calcigenin is in fact described as three RPs quite similar in biological activity—α, β, and γ. Soon after the discovery of co-calcigenin, its extraordinarily powerful peripheral vasodilator properties were identified. Doses of less than 1 pmole (incredibly small, even when compared to doses of other highly active RPs) induce intense expansion of the arterioles of human skin.[22] A sharp jump in overall circulation in the extremities has been described. In systemic administration of the preparation in doses of 1-10 μg/kg, significant expansion has been observed in the celiac and coronary arteries, as well as in the cerebral vessels.[18,22,32] The duration of action is measured in hours. Even more pronounced effects are noted when co-calcigenin is combined with substance P: the vasodilation is accompanied by leukocytic diapedisis. This combined effect apparently reflects their role in neurogenic inflammation processes.

It is still too early to place a number of other effects of co-calcigenin that are of considerable interest in terms of fundamental theory and practice into the category of rapid and strong.

Unlike the most powerful effects of many other RPs, which manifest themselves in pathological states, the vascular effects of co-calcigenin can also be clearly tracked in a healthy body.

Atriopeptides. The family of atriopeptides is rather large. Here we are looking at the effects of only the generally acknowledged leading RP of this family, which consists

of 28 amino acid residues. The powerful diuretic and natriuretic action of small doses (in micrograms per 1 kg) of systemically introduced atriopeptide-28 has been thoroughly proved: diuresis and natriuresis are ten times greater than the norm in experimental animals and in humans.[2,47] This effect occurs in the norm as well as in pathology (especially when fluid balance is disturbed as a result of cardiovascular insufficiency). Effects similar in strength are found in, for example, a powerful nonpeptide diuretic such as furosemide. A pronounced effect with furosemide, however, is achieved only in doses that are 100 times larger and is accompanied by unwanted potassium uresis rather than the natriuretic effect of atriopeptide-28. The duration of action of the latter in clinical conditions, in intravenous administration of 5 μg/kg is about two hours.[47]

Other effects of atriopeptide, including a lowering of diastolic pressure, are not so pronounced.

Vasopressin is an atriopeptide antagonist and has long been known as a powerful antidiuretic. Using it to produce the pressor effect requires the use of substantially larger doses. There is even less reason to label as strong effects those such as lowering of body temperature, bradycardia, and strengthening of memory consolidation, although their predictability and importance are obvious.

Neuropeptide Y has a strong vasoconstricting effect, including in peripheral arteries and coronary cerebral vessels.[23,41,43] It induces a substantial and rather long-lasting rise in arterial pressure. In extremely delicate clinical experiments, this same effect was noted in people given doses of up to 5 μg/kg.[19] Neuropeptide Y is a powerful stimulator of food-seeking behavior in rats.[35]

Oxytocin. As earlier, only stimulation of contractions of the uterus and secretion of milk during breast-feeding can be considered strong and rapid effects of oxytocin. The important behavioral effects of oxytocin established over the last ten years (such as the effect on maternal behavior, the recall process, and sexual behavior) are manifested predominantly in central administration and, as a rule, cannot be classed as strong and rapid.[33]

Hibernation peptides. Lowering of the body temperature and suppression of the energy metabolism has been recorded with many RPs. These effects are manifested, however, primarily in central administration (such as bombezin [not further identified], neurotensin, and cholecystokinin). The results of systemic administration are less significant and are not always reproducible. For now, strong and rapid lowering of body temperature and energy metabolism are described only for the hibernation peptide (or peptides)[9, 10] taken from the bodies of susliks and "double-breathing" fish. Although the effects of these preparations are considerable, they have yet to be completely identified.

Other RPs about which data exists on rapid and strong physiological effects. The list of such RPs is large. We will examine only three groups of peptides that can be considered the most suitable "candidates" for the category of strong, rapidly acting peptides.

The vaso- and bronchodilating action of vasoactive intestinal peptide (VIP) was described rather long ago. In doses of 1-10 μg/kg, systemically administered VIP causes a lowering of arterial pressure; there are indications of dilation of peripheral and cerebral vessels.[26,42] In strength, these effects can be considered medium. It is not out of the question, however, that, as with the RPs described above, pathological states can be identified in which the action of VIP is more pronounced. A pronounced weakening effect on the musculature of the bronchi in animal experiments prompted clinical trials in the use of VIP to arrest asthmatic symptoms.[20] At the moment, however, the findings cannot be considered conclusive. It is possible that the abundance of proteases in the bronchial secretions of asthmatics serves as a barrier, which would accelerate the decomposition of externally introduced VIP. If that is so, then strong effects can be expected when VIP is administered with protease inhibitors. The other effects of VIP—such as hypnogenic and immunotropic effects—cannot be classified as strong either.

In terms of strength and speed of action, tachykinins merit lasting attention. Rather manifest is the induction by these RPs of a number of elements of the inflammation process, such as vasodilating action (especially on veins) and bronchospasmatic action.[27,38,40] The effect of tachykinins on the nociceptive reflex is complex.

The adaptive, antistress action of substance P is well studied. For all the importance attending the effect, however, it would be difficult to classify the effect as rapid and strong.

Convincing evidence has been accumulated over the last five years for the ability of cholecystokinin-8 to suppress food-seeking activity in animals not only with central administration, but also with systemic administration.[50] In addition, the effects on certain behavioral responses—such as relieving withdrawal in alcoholics and a number of other effects—can be placed in the category of strong and rapid effects.[3]

It has already been emphasized above that the effects of natural RPs in central administration are excluded from the examination, that attention is focused on strong and rapid physiological—but not biochemical—effects, and that definite limitations have been be introduced involving duration of action. As a result, we have not examined such large groups of natural RPs as opioids or such popular groups of RPs as angiotensin II and bradykinin. Obviously, further study of the properties of the RPs known at present, especially in connection with their action in pathological states, will lead in the near future to an expansion of the list of strong, rapidly acting RPs.

Is the creation of RP analogs a necessary stage on the road to their being introduced into practice? We, of

course, have no doubt of the advisability of persistent, steady work in the creation of analogs that either surpass the natural RPs in stability and duration of action, or have a modified spectrum of activity that is more adequate for given therapeutic tasks, or, finally, combine all such advantages. The substantial achievements on this road are generally acknowledged. At the same time, one cannot fail to note that introducing not the natural RP, but its analog, requires greater care and preclinical tests of greater complexity to evaluate its harmlessness and to identify possible new types of activity. The material presented above on the strong, rapid, comparatively long-lasting effects of natural RPs in certain pathological processes enables us to consider as advisable further persistent study of their therapeutic potential. We again point out that this is true in regard not only to medium-sized RPs that consist of 20-40 amino acid residues, but also to a number of small RPs. Experience in the use of one-time injections of a tripeptide such as TRH is impressive. Its varied effects, which last hours and sometimes even longer, cannot be explained merely by stimulation of thyrotropin and the subsequent release of thyroid gland hormones. Apparently, this short-lived RP triggers other kinds of regulator systems and cascades. This probably also explains the long-lasting effects of a number of other small RPs: such as cerulein, neurotensin, and tetrapeptidamide analog of enkephalin.[7,15,24,34] And as far as medium-sized RPs go, their duration of action (hours) is of practical interest in certain situations, even without any consideration of possible chain reactions. Finally, new possibilities that facilitate repeated (and even initial) use of many RPs are opening up as a result of the fact that they are highly effective when administered intranasally. At present, the list of RPs that are effective in humans when they are administered in this manner includes vasopressin, oxytocin, TRH, somatoliberin, atriopeptide-28, opioid peptides, and $ACTH_{4-10}$.[45,46] Moreover, animal experiments indicate this route of administration to be effective for tuftsin, an analog of $ACTH_{4-9}$, and dermorphine. As a rule, the duration of the effects in intranasal administration is equivalent to that in parenteral administration, and sometimes even is higher.[45,46] Certain features of the activity spectra have also been noted in this method of administration.

Thus, the combination of strength and speed of effect with a duration of action that often lasts hours (or longer) and with the possibility of repeated intranasal administration opens new horizons for the use of natural RPs as such in certain pathological states. These very data not only do not preclude further investigations of new analogs of RPs—they serve as an impetus for them.

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UDC 612.438+616.45—001.1/3

Influence of Thymus and Bone Marrow Polypeptides on Morphofunctional State of the Rat Thymus After Stress

18400020 Alma-Ata IZVESTIYA AKADEMII NAUK KAZAKHSKOY SSR: SERIYA BIOLOGICHESKAYA in Russian No 3, May-Jun 88, pp 88-93

[Article by T. K. Supiyev, I. M. Voropanov, I. I. Grintsevich, V. Kh. Khavinson, and V. G. Morozov, Alma-Ata State Medical Institute, KaSSR Ministry of Health]

[Abstract] A study is presented of the influence of "timogemin"—a complex thymus and bone marrow immunomodulating polypeptide preparation—on the morphofunctional states of the rat thymus after combined mechanical and cold trauma. Experiments were performed on 96 male white rats, selected for cold resistance. Some of the rats were administered 5 mg/kg timogemin, extracted from the thymus and bone marrow of calves by acetic acid extraction and subsequent ion-exchange chromatography. Administration of timogemin three times caused a reduction in the dimensions of the lobes and in the thickness of the cortical matter of the thymus, with clear lamination of the thymus lobes, but no appreciable change in mitotic index. After two weeks, the morphologic changes in the thymus in rats receiving

timogemin had disappeared. The mitotic index, however, increased still further. The number of cell components per unit area of lobe returned to normal. It is concluded that hypothermia inhibits the reaction of the thymus to stress, which is confirmed by the low macrophage reaction in the cortical substance of the thymus lobes and low mitotic index in control rats. Administration of timogemin increases the functional activity of the thymus after three days and produces a reliable increase in the number of small lymphocytes and the number of mitoses after one and two weeks, which may be due to intensified proliferation and differentiation. References 11: 9 Russian, 2 Western.

UDC 577.352.46

Influence of Met-Enkephalin on Glutamate Release and Uptake in Rat Striatum

18400031a Yerevan NEYROKHIMIYA in Russian Vol 7 No 1, Jan-Mar 88 (manuscript received 27 Apr 87) pp 11-17

[Article by O. V. Godukhin, S. I. Zharikov and A. Yu. Budantsev, Institute of Biological Physics, USSR Academy of Sciences, Pushchino]

[Abstract] Enkephalins inhibit the release of noradrenaline, dopamine, and acetylcholine, thus acting as presynaptic regulators of neurotransmitter release from neuron endings. It is not clear whether these substances inhibit the release of all neurotransmitters or only catecholamines and acetylcholine. The influence of Met-enkephalin on the release and uptake of glutamate (an important neurotransmitter in the brain) at presynaptic endings was studied with a technique that used local superfusion of the rat neostriatum. Use of a push-pull cannula made it possible to record the electrical activity from the area being superfused. At a concentration of 10^{-6} M, Met-enkephalin had no reliable influence on spontaneous release of ^{14}C-glutamate. Release caused by high K^+ concentration in the medium, however, was inhibited when the Met-enkephalin concentration was at 10^{-7} M. Met-enkephalin had no effect on Na^+-dependent uptake of ^{3}H-glutamate. The findings indicate that Met-enkephalin is a presynaptic inhibitor of the stimulated release of glutamate and other neurotransmitters in the brain. Figures 5, references 9: 3 Russian, 6 Western.

UDC 578.858

Varying Influence of -Interferon on Rat Brain and Opiate Receptors

18400031b Yerevan NEYROKHIMIYA in Russian Vol 7 No 1, Jan-Mar 88 (manuscript received 17 May 87) pp 73-77

[Article by T. N. Alyabyeva, A. M. Balashov, and L. F. Panchenko, All-Union Scientific Research Center for Medical-Biological Problems of Prevention of Alcohol Abuse and Alcoholism, Moscow]

[Abstract] The structural similarity of the molecules of β-endorphin and α-interferon suggests that α-interferon has opioid activity. Central administration of α-interferon, like β-endorphin, causes analgesia and catatonia and suppresses spontaneous motor activity, i.e., leads to development of opiate-like effects, which are prevented or changed by administration of naloxone. This article attempts a detailed study of the binding of α-interferon with cerebral opiate receptors in the rat, focusing on the effects of small doses. The α-interferon appears to combine with two segments on the opiate receptor complex—with the binding receptor center itself and with an α-interferon center that represents an allosteric regulator segment. The fact that relatively small concentrations of α-interferon cause ^{3}H-naloxone to interact with the receptor suggests that α-interferon has greater affinity for an allosteric center than for the active receptor center. The data indicate possible presence on the opiate receptors or in their immediate surroundings of an allosteric regulator center, as previously suggested by the authors. The precise location of the center (or centers), its nature, and the specifics of interaction with the regulators are not known. Figure 1, references 10: 4 Russian, 6 Western.

UDC 612.8+612.014.42+612.615.2

Effect of Synthetic Encephaline Analogue (Dalargine) on Pulsed Activity of Positively Reinforcing Zones of Rat Hypothalamus

18400026 Moscow ZHURNAL VYSSHEY NERVNOY DEYATELNOSTI IMENI I. P. PAVLOVA in Russian Vol 38 No 2, Mar-Apr 88 (manuscript received 17 Apr 87) pp 378-380

[Article by N. G. Mikhaylova and M. I. Zaychenko, Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow]

[Abstract] Dalargine—an analogue of dinorphine fragment synthesized at the All Union Cardiologic Center—facilitates regenerative processes in ulcerating gastro-intestinal tract. Also, it exhibits hypotensive properties. Effect of dalargine on neuron action of lateral hypothalamus (LH) and the lateral preoptic region (LPR) was investigated on male rats. Experiments on unrestricted, alert rats showed that systemically administered dalargine showed a dampening effect on spontaneously active neurons of LH and LPR in the majority of cases. This peripheral effect of dalargine may be related to its direct action on hypothalamic structures or be an indirect effect through an action on the antinociceptive brain system. Figure 1; references 5: 4 Russian, 1 Western.

UDC 612.812

Effects of Regulatory Peptides on Recovery of Visual Functions in Retinitis Pigmentosa

18400030a Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 14 No 1, Jan-Feb 88 (manuscript received 9 Dec 86) pp 43-49

[Article by N. B. Kostelyanets, O. B. Ilyinskiy, I. A. Shevelev, R. F. Yeliseyeva, L. A. Katsnelson, M. I. Titov, and G. I. Dnestrova, Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences; Scientific Research Institute of Eye Diseases imeni Gelmgolts, RSFSR Ministry of Health; All-Union Cardiologic Scientific Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] Therapeutic trials were conducted with dalargin (leu-enkephalin) to assess the effects of its intramuscular and subconjunctival administration on the status of visual function in patients with retinitis pigmentosa. The cohort consisted of 37 male and female patients, 21 to 57 years old, with a 1-to-21 year history of the disorder. The patients were tested for visual acuity, field of vision, ERG, contrast sensitivity, and differential light threshold. Treatment consisted of 1 mg dalargin intramuscularly and 0.3-0.5 mg subconjunctival [sic] per day for 7 days. Evaluation of the function tests 6 months after the therapy showed significant improvements in two of the parameters tested. Visual acuity was significantly improved in 70 percent of the patients and contrast sensitivity in 93 percent. In addition, 20 percent of the patients presented with an expansion of the field of vision. The effects of the synthetic peptide in improving impaired vision was felt to be due to mechanisms involving excitatory (dopaminergic) and inhibitory (GABA and glycine containing) amacrine cells. The role of dalargin appears to be that of a trigger mechanism since its halftime is on the order of 2 min. Figures 2; references 28: 16 Russian, 12 Western.

Altered States of Consciousness in Healthy Subjects: Definition and Prospects in Research

18400030c Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 14 No 1, Jan-Feb 88 (manuscript received 26 Mar 87) pp 138-147

[Article by L. I. Spivak, Institute of Experimental Medicine, USSR Academy of Medical Sciences, Leningrad]

[Abstract] Altered states of human consciousness have received considerable attention in recent years. In the West, thousands of papers have been published that deal in one way or another with this subject, whereas, in the USSR, the number of articles has been limited to 15 or less, and includes one monograph. Most of the publications and research dealing with altered consciousness has been phenomenological in nature. Nevertheless, despite the limited information on neurophysiological and neurochemical correlates attendant to this state, there has been a gradual reorientation of research directions with greater emphasis on the physiological substrate of consciousness. EEG parameters have been found to be altered in a number of situations with an altered state of consciousness, e.g., hypnosis, sleep stages, creative endeavors, emotional distress, etc. While the information is preliminary and subject to variable interpretations, it has become clear that studies on altered consciousness open up a new avenue in brain studies that may provide a better understanding of mental adaptation, psychopharmacology, and borderline personality disorders. References 34: 26 Russian, 8 Western.

UDC 617-001.32-001.36-085.243[547.95:547.943

Influence of Enkephalin Analog Dalargin on Course of Severe Compression Shock

18400034a Moscow PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA in Russian No 2, Mar-Apr 88 (manuscript received 14 Jan 87) pp 15-18

[Article by G. K. Zoloyev, Laboratory of Pathophysiology, headed by doctor of medical sciences V. D. Slepushkin, Siberian Affiliate, All-Union Cardiologic Scientific Center, USSR Academy of Medical Sciences, Tomsk]

[Abstract] A study is presented of the influence of dalargin on the course of compression shock under experimental conditions. Experiments were performed on 165 male white rats and 170 male white mice, with compression shock modeled by vise compression of the lower extremities for seven hours, with IV (rats) and intraperitoneal (mice) administration of dalargin. The levels of calcium, magnesium, glucose, and urea in the blood were then determined, as well as those of ATP, ADP, and AMP in liver tissue. The results indicated that the hexapeptide dalargin has a significant effect on the course of severe compression shock in the early stages, improving peripheral circulation, but possibly reducing the contractile function of the myocardium. In the later stages of shock, dalargin is ineffective and may even worsen the course of the pathological process. The overall effect of the preparation, however, is positive, indicated by the lower mortality rate among the animals receiving dalargin. References 12: 10 Russian, 2 Western.

UDC 616-005.1-06:616-001.36]-085.835.12-036.8-07:[616.1-008.1+616.152.11+616.74-008.922.1

Regional Circulation, Redox Potential, Oxygen Tension and Consumption in Skeletal Muscles in Hemorrhagic Shock and Hyperbaric Oxygenation

18400034b Moscow PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA in Russian No 2, Mar-Apr 88 (manuscript received 25 Nov 86) pp 18-20

[Article by V. A. Kuznetsov and A. N. Leonov, Department of Pathologic Physiology, headed by Professor A. N. Leonov, Voronezh Medical Institute imeni N. N. Burdenko]

[Abstract] A study is made of the influence of hyperbaric oxygenation on regional circulation, oxygen tension (pO_2), oxygen absorption, redox potential and effectiveness of oxidative phosphorylation (P/O ratio) in muscle tissue in experimental hemorrhagic shock. Studies were performed on 235 white rats after 20 ml/kg (plus or minus 2.2) blood were drawn from each, causing arterial pressure to drop to 51 mmHg (plus or minus 2). Hyperbaric oxygenation was performed at 3 atm. abs. for 50 minutes. The results were statistically processed. The

results indicated that hyperbaric oxygen prevents excessive (pathologic) stress on the mechanisms of circulatory centralization and ensures optimization of overall and regional hemodynamics. The oxygen supplied to the internal organs was maintained without hypercompensatory changes in the central and peripheral circulatory systems, since oxygen saturation of the tissues occurred as a result of the increase in the tension of oxygen physically dissolved in the blood and the increase in diffusion of oxygen to the cells due to hyperoxygenation. Figure 1, references 8: 7 Russian, 1 Western.

UDC 612.17+612.53+577.15/.17

Action of Immunostimulator Tuftsin on Heart Rate and Body Temperature of White Rats

18400064 Leningrad FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I.M. SECHENOV in Russian Vol 74 No 4, Apr 88 (manuscript received 21 Jul 86) pp 547-550

[Article by A. A. Kamenskiy, N. Yu. Sarycheva and V. N. Kalikhevich, Complex Laboratory of Biology Faculty (Director G. O. Lilp), State University, Moscow]

[Abstract] The tetrapeptide tuftsin (Thr-Lys-Pro-Arg) was first isolated from the leucophylic fraction of immunoglobulin and studied as a nonspecific immunity stimulator. Effect of tuftsin on vegetative indices of the body was examined on 80 white male rats. At a dose of 0.3 mg/kg/ tuftsin exhibited a positive chronotropic effect on the heart rate when administered in the state of low heart rate; at a higher basal rate, a bradycardic response was noted. Concerning body temperature, administration of tuftsin resulted in a 5 min transient hyperthermia followed by a longer period of hypothermia and then restoration to the basal level. During the hypothermia phase, mobility of the rats decreased along with emotionality; conditioned reflex time was slowed down. When reserpine injection preceded tuftsin, no hyperthermic effect was noted, but some potentiation of hypothermia induced by reserpine was observed. The changes in vegetative indices evoked by tuftsin show a phasic nature and their direction depends on the initial functional state of the animal. Figures 2; references 10: 5 Russian, 5 Western.

UDC 612.821.3:66

Technical Control System Failure as Indicator of Physiological Stress in Control Operators

18400067a Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 14 No 3, May-Jun 88 (manuscript received 9 Dec 86) pp 424-427

[Article by M. A. Gritsevskiy, L. S. Bashkirova, T. N. Dolgolenko, Yu. V. Yegorova, V.V. Glotov and S. A. Kolesov, Institute of Labor Hygiene and Occupational Diseases, Gorky]

[Abstract] A 3-year study was conducted at a new ethylene oxide plant to access the relationship between the incidence of system failure and physiological stress in controllers and equipment maintenance personnel. The physiological parameters included evaluation of visual-motor reactions, attentiveness, electrocardiography, mobility of visual analyzer, blood pressure measurements, and differential blood counts. The working conditions, involving as they did anticipation of system problems and demanding immediate corrective measures, showed that the probability of failure served as an indicator of occupational stress. Over the 3-year period, the probability of system failure in the different categories fell from an initial 0.34-0.7 to 0.1-0.11, and was accompanied by physiological evidence of abatement in stressful activation of the CNS. It became evident that shortcomings in the technological plans were responsible for worker stress, based on their anticipation of problems in the production of ethylene oxide. In addition, unfamiliarity with the production process, inadequate training, and inexperience were also major factors leading to what may be in some cases avoidable stress. Consequently, situations such as these require more refinement to optimize performance efficiency through closer attention to ergonomic and other factors. References 8 (Russian).

UDC 612.821.1/3+612.122.53

Local Heat Loss as Wakefulness-Maintenance Factor in Monotonous Human Activity

18400067b Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 14 No 3, May-Jun 88 (manuscript received 13 Apr 86) pp 428-433

[Article by I. S. Shenderova, Institute of Labor Hygiene and Occupational Diseases, Gorky]

[Abstract] A study was conducted on 7 individuals to assess the effects, if any, of local heat loss on wakefulness. The laboratory studies involved application of a 5.3 cm^2 heat sink to the skin of the frontal lobe, with a 5 degree C temperature difference between the applied plate and the skin. Heat loss was employed after 30 min of a monotonous task after the onset of monotony as indicated on the 'Level of Wakefulness' scale. Psychometric and physiological parameters demonstrated that the induction of local heat loss led to greater alertness and improvements in physical and mental performance. A similar trial, conducted with 23 drivers, led to marked improvement in the alertness of 15 (65.2 percent), no effect in 5 (21.7 percent), while evaluation was not completed in the case of 3 individuals (13.0 percent). These observations appear to be particularly valuable in case of subjects engaged in monotonous tasks and shown to be susceptible to diminishment of wakefulness under such conditions. An apparatus is currently under development that will employ the heat-loss principle in maintaining wakefulness. Figures 4; references 20: 19 Russian, 1 Western.

UDC 612.766.1

Dynamics of Differential Thresholds of Sensory Analyzers During Processing Activity

18400067d Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 14 No 3, May-Jun 88 (manuscript received 10 Apr 87) pp 510-512

[Article by V. N. Sysoyev, Military Medical Academy imeni S. M. Kirov, Leningrad]

[Abstract] An analysis was conducted on the efficiency of information processing in the course of task accomplishment, involving auditory, visual, and motor analyzers in 300 men between the ages of 19 and 22 years. The subjects were required to perform various tasks differing in difficulty. The results demonstrated that as the duration and work load increased the discriminatory thresholds of the auditory and motor analyzers decreased. The differential sensitivity of the visual analyzer, however, remained unaffected under analogous conditions. The differences in the behavior of the sensory analyzers under consideration are evidently due to the prevalence of different programs in the central nervous system for processing the corresponding sensory inputs. References 13: 9 Russian, 4 Western.

UDC 362.7+362.172(575.4)

Ways of Restructuring the Service for Protection of Maternity and Childhood in the Turkmen SSR

18400039 Ashkhabad ZDRAVOOKHRANENIYE TURKMENISTANA in Russian No 4, Apr 88 pp 3-6

[Article by Turkmen SSR Deputy Minister of Health S. G. Yusupov]

[Text] Continued improvement of the organization of medical care for women and children was defined as a priority of Soviet health care in the "Basic Guidelines of Developing Public Health Protection and Restructuring Health Care in the USSR in the 12th Five-Year Plan and in the Period up to the Year 2000."

In our republic, which has had the country's highest mortality rates for infants and mothers and one of the highest birth rates for a number of years, protection of maternity and childhood has special importance.

In recent decades the priority attached to the service for the protection of the health of the mother and child has diminished, and as a result of this the material and technical base has fallen significantly behind, an acute personnel shortage has been created, there are serious problems in job training, and there are unsolved problems in managing the diet of children in their first year of life. The year 1986 was a turning point, a unique landmark in the development of protection of maternity and childhood in the republic.

Creation of a republic commission on the problems of motherhood and childhood under the Turkmen Communist Party Central Committee, and of commissions under the party oblast, city and rayon committees, made it possible to work together with party and soviet organs and various ministries and departments to develop a broad program for further improvement of the protection of motherhood and childhood in Turkmenia.

The plan for economic and social development in the 12th Five-Year Plan provides for introducing hospitals with a total of 5,770 beds, to include 1,820 beds at the expense of kolkhozes, sovkhozes, union ministries and departments. Forty-one percent of the total are to be reserved for children and obstetric care (the figure in previous five-year plans was 8-10 percent).

At the same time the material base of the health care sector in the republic is not satisfying the population's needs today. Almost 60 percent of the hospitals and polyclinics are still housed in ill-suited, crowded buildings, without adequate plumbing. According to the standards there should be 46,800 beds in operation, but the shortfall is around 10,000 beds. Of these, 7,000 belong in children's and obstetric institutions (3,000 obstetric and gynecological and 4,000 children's beds, predominantly in infectious wards).

Eight thousand children's and obstetric beds, plus polyclinics for children and for women's consultation services with a capacity of 11,000 visits per shift, are to be introduced in accordance with the draft of a special program for sociocultural development in the 13th Five-Year Plan.

This is the second year that locally initiated construction of social, cultural and personal service facilities has been going on in the republic's rural areas. Over 90 health care facilities (chiefly SVA and FAP [not further identified]) are now under construction. Over 4 million rubles have been earmarked for these purposes in 1988. Part of this money will be used to renovate existing hospitals. However, except in Chardzhou Oblast, this means of strengthening the base of rural health care is being utilized insufficiently, and oblast health care divisions need to approach the problem more seriously.

Because the material and technical base is lagging behind, the availability of medical personnel is low as well. An alarming situation has evolved in the republic in regard to the quality of physician training. Despite the fact that the number of pediatricians grew from 10,700 for every 10,000 children in 1985 to 14,000 pediatricians in 1987, and obstetrician-gynecologists grew from 1,800 per 10,000 residents to 2,300, the shortage of physicians in these specialties remains significant.

Graduation of obstetrician-gynecologists from the TODNGMI [not further identified] has now increased from 30 to 70. Beginning in 1988, graduates of VUZes in the RSFSR and the Ukraine will be sent to Turkmenia on an annual basis (30 pediatricians and 15 obstetrician-gynecologists), and 60 pediatricians and 25 obstetrician-gynecologists from among TODNGMI graduates will be sent to central institutes for their internship.

Steps are being taken to upgrade the qualifications of pediatricians and obstetrician-gynecologists. Since 1986, only the TuSSR Ministry of Health has been certifying physicians prior to awarding them certification categories. In addition to the republic scientific-practical conferences and seminars conducted annually, central institutes are organizing traveling advanced training courses for physicians: this year alone six such courses have been provided, and over 200 physicians have undergone training. No less than five traveling courses will be organized in 1988. In the last 2 years, 130 obstetrician-gynecologists received instruction in basic surgical interventions, which has made it possible to maintain a surgical specialist in every rayon in the republic.

Pediatricians, obstetrician-gynecologists and middle-grade medical personnel of children's and obstetric institutions were tested in 1987. As a result, 30 physicians were relieved of their positions and transferred to other work unrelated to therapeutic practice, around 20 were placed on probation, and 70 physicians were enrolled in advanced training courses. This work will continue into the future.

The level of proficiency required of students undergoing training in the TODNGMI was reviewed. Thus, 234 students were dismissed in the 1986-1987 school year because of poor proficiency. This is three times the number in previous years. Also, instead of receiving physician's qualifications, three graduates were accorded the qualifications of a middle-grade medical worker on the basis of the results of state examinations in 1987.

Priority measures have been taken to staff rural health care institutions with pediatricians and obstetrician-gynecologists. While in 1986 only 50 percent of the pediatricians and 55 percent of the obstetrician-gynecologists of the TODNGMI's graduating class were sent to rural areas, in 1987 the figures increased to 70 and 76 percent, respectively.

The regional features of our republic (low population density,territorial isolation of population centers, low availability ofphysicians, demographic features, etc.) compel us to seek neworganizational forms of medical service for women and children.

A nonstandard, flexible, creative approach to today's problems in pediatrics and obstetrics that takes into account local conditions is one of the principal ways of restructuring the activities of the service.

Considering the high birth rate, health care organs and institutions have been given the opportunity to introduce obstetrician-gynecologist positions into the staffs of SUB and SVA, irrespective of their bed capacity and the size of the population requiring services. In this connection, rural health care will receive around 300 additional physicians of this specialty in the next few years.

All families with children a year old or younger have been granted the right to obtain free children's food products, regardless of material status.

Significant expansion of the network of resuscitation wards represents a serious step in the improvement of the medical assistance provided to the republic's population. In the last 2 years, 42 resuscitation and intensive care wards were created in city and rayon hospitals, and another 13 are being organized. These wards have been provided with additional instruments and equipment. Physicians are undergoing special training during their internship and on the job in regard to the problems of resuscitation and intensive care. Permission to organize resuscitation wards in all central rayon hospitals and in a number of maternity hospitals, irrespective of bed capacity, was granted in an order of the TuSSR Council of Ministers. All resuscitation wards have reserved two beds for treatment of children. As quickly as possible, these wards need to be furnished with modern medical equipment and highly qualified specialists must be trained for them.

In order to reduce the high level of sudden infant death syndrome in children during the first year of life and infant mortality in the home, in 1985 the city of Ashkhabad created an emergency care station for the treatment of seriously ill children up to 2 years old whose parents refuse to hospitalize them. This organizational form of work has been found to be effective and has been extended to all of the republic's territory. Seventeen emergency care and resuscitation stations are now functioning successfully in children's hospitals and polyclinics. Steps are being taken to improve first aid and emergency care for children. In the last year and a half the number of pediatric brigades increased from 29 to 49.

These measures made it possible to reduce the level of sudden infant death syndrome and infant mortality in the home by a factor of over 1.5.

The health of an infant depends on many factors, chiefly the health of the mother, her diet, and her working and living conditions. But doctors alone cannot solve all of the problems associated with a mother's health. We need to consolidate the efforts of the party committees, the soviets of peoples deputies and the trade union organs.

Research has shown that 50-70 percent of mothers hospitalized in order to care for sick children suffer from various illnesses themselves. In this connection all of the republic's children's hospitals began an effort in 1986 to improve the health of mothers. Therapeutic wards were opened in the NII OZMR [not further identified] with 60 beds and in the Tashauz Oblast Children's Hospital with 30 beds.

Extra physician-therapist positions have been introduced at all children's hospitals, and the Statute on Restoring the Health of Mothers Hospitalized to Care for Children in All Children's Wards was written. Over 10,000 women received this form of treatment in 1987.

The practice of establishing day hospitals has asserted itself more and more decisively in recent years. Around 30 beds for the treatment of different forms of pathology associated with pregnancy were set up in Ashkhabad at the NII OZMR and at women's consultation offices. The treatment results demonstrate the high effectiveness of this form of work, which is especially important in view of the bed shortage.

Preventive work among women and children remains at a low level. Special attention must be devoted in this regard to the grass-roots level—the FAP and SVP—which are not providing for regular, frequent check-ups of children and pregnant women.

Steps are now being taken to assign all children in their first year of life to specific medical workers, who must provide home health care to the children no less than two to three times a week.

Oral rehydration was carried out everywhere in the summer months of 1987 in order to reduce the occurrence of intestinal infection. All children up to 1 year of age were provided with drugs for oral rehydration (oralit, regidron). These measures made it possible to prevent the growth of child mortality in the summer period in most of the republic's oblasts. Proper management of this work, in addition to the provision of regular, frequent check-ups of children in their first year, should be seen as one of the most effective measures for reducing child mortality.

Steps have been taken to improve the diet of children. In the last one and a half years, production of formula by dairy kitchens was increased by 10,000 portions, and in 1987 deliveries of dry formula increased to 1,100 tons in the republic (only 682 tons were delivered in 1986). Construction of a baby food department capably of producing of 22,000 portions has been completed at the Ashkhabad City Dairy; it will begin production soon.

In rural areas, the bulk of dry formula is acquired by central rayon hospitals and distributed free to children in their first year; in the cities, however, this formula is sold commercially, and it is not always used for its intended purpose. A decision was made in this connection to have stores supply dry formula free, on prescription.

Practically speaking, the republic does not have a family planning service, even though this is precisely the locus of one of the main causes of high infant mortality. "Marriage and family" consultation offices have been created in all oblasts, and efforts to reduce the number of abortions and to introduce modern methods of contraception are becoming more vigorous. The NII OZMR has created a family planning center which should become the organizer and coordinator of work on this problem.

The problems facing the service for protection of the health of the mother and child are enormous, and their importance is understood by all. The main task today is to transform the energy of our thoughts more vigorously into the energy of action, since the success of our common cause depends on the contribution of every individual, on his civic pride, and on his job proficiency.

UDC 616-084.3

Some Problems Associated With Improving Specialized Medical Care

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[Article by G. Z. Demchenkova and N. P. Soboleva, All Union Scientific Research Institute of Social Hygiene and Health Care Managment, USSR Ministry of Health, Moscow]

[Text] The resolutions of the 27th Congress of the CPSU devote special attention to the protection of public health. Effecting a system of measures to preserve and strengthen the health of the population is one of the most important social tasks assigned by the Party. To a large extent, the continued development and improvement of preventive work and the introduction of mass health screening of the entire population will facilitate the successful execution of the task. Mass health screening here means a single integrated system that ensures a comprehensive evaluation of the state of public health, the active monitoring of the health of every individual, and the combined accomplishment of socioeconomic and medical measures for improving working and living conditions.

The transition to mass health screening of the entire population is a complex process that touches all areas of the health care sector. In order to successfully handle the task of changing over to universal screening, the treatment and prevention facilities and the scientific research institutions of the country are developing new approaches that ensure fuller and better medical, staff, and technical solutions to the problem. Scientific research conducted over a number of years in the organization of annual mass health screening of the entire population has made it possible to amass considerable experience, to develop new organizational forms and methods of annual screening, and to identify indices for the volume of work performed by physicians of various specialties and diagnostic services. The order enacted by the USSR Ministry of Health "On the Procedure for Conducting Mass Health Screening of the Population" is, in fact, the primary guideline for carrying out the screening.

The current stage of the transition to mass health screening involves the development of specialized medical care, at the basis of which is the improvement of the structure and activity of outpatient polyclinical institutions and the introduction of progressive organizational forms of the active monitoring of patients and individuals at risk, the newest diagnostic and treatment techniques, and greater efficiency of labor among physicians and mid-level medical personnel. Playing an important role in the accomplishment of this set of tasks is the creative collaboration between workers in the theoretical and applied sectors to introduce the achievements of science into health care practice in a timely manner and on a broad basis.

In spite of the fact that the number of those screened increases in mass health screening, especial attention must be given here to the quality of the active monitoring of patients. Raising that quality facilitates the development of specialized medical care and the participation of physicians of various specialties in the screening of the patients. The help given by specialists from the departments of specialized scientific research institutes will, to a large extent, also help improve the clinical observation of patients and raise the effectiveness of mass health screening.

The sharp increase in the number of physicians with specialties has resulted in the need for the very closest of interaction among them not only in science but also in

practical health care, because without that interaction neither management and administrative problems nor problems associated with raising the quality of the specialized care rendered to the population can be solved.

The interrelated and logical processes of specialization and integration that take place in medical science and health care practice determine the organizational forms for rendering different types of medical care to the population, have a substantial influence on the structure and functions of institutions such as outpatient polyclinics and hospitals, and determine the organizational forms and methods of the work done by specialized services in mass health screening.

Mass health screening of the entire population is possible only with the creation of a well-balanced functional and diagnostic system in which the district service takes a leading role in integrating all the health care services as well as many of the sectors of the national economy.

The task at hand is to create in the long term an integrated health care system based not on the public's seeking outpatient polyclinical care in a haphazard manner, but on the steady active monitoring of the state of health of the entire population, on the active identification of illness at the very earliest stages, on complete integration of prevention and treatment at all health care institutions, and on the continuity and coherence of the work associated with protecting and strengthening health at all stages of an individual's life—during infancy, childhood, and adulthood.

The integrated nature of the district-centered model for the territorial level makes it possible to concentrate the work of mass health screening in the hands of the district physician, who is called upon to organize the complex combination of preventive and treatment-and-diagnostic processes in terms of the patients in the district. Controlling the screening, the district physician must work closely with all kinds of specialists, and not just with medical specialists. He is rightfully the leading figure, the primary organizer and coordinator of the screening work among the physicians of all the specialties.

Playing an important role in the annual clinical checkups of the entire population is the district-team method (specialized district center), the essence of which consists in the interrelated, coherent work of physicians of various specialties with the district physician. This method is one of the most progressive means of improving the quality of the screening and of solving the complex problems associated with specialization and integration of extrahospital care today. Having various specialists work together in a single department eliminates duplication in the examination of individuals who are under clinical observation, keeps consultations from dragging out several days, and, in addition, gives specialists the opportunity to better acquaint themselves with the residents in the individual districts and to systematically conduct team evaluations of their own work.

The transition to mass health screening of the entire population requires the organization of the closest interrelationships and interdependences of skilled care among the major medical specialties at the check-up stage of the entire population, at the specialized service stage — when those in need undergo preliminary examination—and when they and others undergo further mass screening for a given problem. Specialized services must take an active part at all stages of screening, including the organization of operations and measures for preventing given diseases, early detection, treatment, clinical observation, and rehabilitation.

One of the highest priority tasks in the screening of the entire population must be the complex evaluation of the state of health of the population for the purpose of clearly delineating observation groups: healthy individuals, essentially healthy individuals, and the chronically ill. Each group has individuals with risk factors, which provides the basis for determining the effectiveness of clinical observation. The complex evaluation of the health of the population calls for the determination of the condition of individual organs and systems, their functional characteristics, and the level of adaptation of the body as a whole, which requires that unified methods of examination be put into practice. Refining and clearly defining indices for the individual norm and pathology is an important task here. Special attention must be given to risk groups that are based on a complex of risk factors and on subsequent multifactor evaluation of their various fluctuations.

Choosing contingents for clinical observation is the most complicated stage of the screening and requires various organizational and treatment measures. The leading specialists of the polyclinics, together with the district physician, must evaluate the state of health of the population of the region being serviced, conduct an in-depth, multifaceted examination of the state of health of each individual, decide upon the clinical observation groups, compile a list of nosological forms and identify individuals to undergo screening, set up a plan for clinical observation, design the documentation, and assess the effectiveness of clinical observation. In addition to consultation, the specialists must devote a great deal of attention to the screening of the patients, thereby substantially expanding the contingent of those being screened.

Up to now, nosological forms requiring active monitoring were determined by the order of the USSR Ministry of Health "On the Implementation of Instructions for Further Improvement of Screening of Patients in Outpatient Polyclinical Institutions for Adults." The requirements notwithstanding, however, the only patients under clinical observation by specialists are, in essence, those with the leading pathologies. Thus, endocrinologists see those with sugar diabetes, ophthalmologists see those with glaucoma, and rheumatologists see those rheumatic heart disease. In cardiovascular diseases, it was mainly patients with postinfarct damage of the heart and severe hypertension who were taken under active monitoring; in gastroenterological diseases, peptic

ulcer patients accounted for almost 100 percent of those taken under observation.

The introduction of a system of universal screening requires the active monitoring of all patients. Patients must be separated into distinct clinical observation groups based on existing pathology and stage of clinical process.

Expansion of the volume of screened contingents must be conducted according to two criteria: socio-occupational and clinical-physiological. When a patient is taken under clinical observation, factors such as age and sex, part-time or full-time employment, professional affiliation, length of service in chief profession, severity of disease and prognostic possibilities of socio-occupational rehabilitation, and marginal pathology must be taken into consideration. If the quality and effectiveness of the screening is to raised, the complexes of preventive, treatment, and rehabilitation measures that are already developed must use area regional sanatoria and sanatoria-clinics.

The success of the annual mass health screening of the population will depend on the organization of treatment-and-prevention and diagnostic processes at three levels.

The center of the first level is the today's polyclinic, which provides annual check-ups for the population, preliminary examination, and clinical observation within the principal medical specialties.

The second level in the screening is a broad network of specialized centers (offices and departments) that are part of general and specialized interrayon polyclinics and affiliated hospitals. In addition to providing skilled diagnosis and treatment, this level must organize the prevention of specific diseases in the rayon being serviced, perform effective screening of patients, carry out organizational and procedural operations, provide advanced specialty training for personnel, help rayon polyclinics, and enlist the services of academia in consultation work.

The third level of screening consists of specialized centers at clinical institutions and the leading scientific research institutes. They provide scientific and procedural organizational guidance for specialized services on a countrywide basis. The organization of such centers helps considerably to bring about and accelerate the introduction of scientific achievements into practical health care. The centers must play an active role in developing plans for the annual screening of the population of a given area and see to it that such plans are implemented. In turn, the participation of such centers in the annual screening will help to improve the specialized care provided the population.

It is clear that the success of the screening will depend, above all, on the organization of treatment-and-prevention and diagnostic processes in urban general polyclinics in which all the basic forms of extrahospital specialized medical care are concentrated.

At the same time, it pays to organize specialized centers—such as cardiological, rheumatological, ophthalmological, nephrological, urological, allergological, hematological, pulmonological, and gastroenterological—in oblasts and large cities. Setting up such centers helps considerably to bring the topics of scientific research closer to the needs of practical health care and to accelerate the implementation of achievements.

In the annual comprehensive check-ups of the entire population, the work of physicians of different specialties must be interrelated and have continuity: in the preliminary examination of those in need, in the acceptance of patients with similar profiles for clinical observation, and in team monitoring of their state of health. The following measures must be taken: groups which require check-ups by physicians of related specialties must be delineated in the population, based on age, sex, profession, presence of risk factors, and nature and degree of risk factors; a list of nosological forms that require team examination and treatment must be compiled; good lines of communication must be established; and a unified evaluation of the effectiveness of the clinical observation of patients with related profiles must be introduced.

The integrated nature of the work of physicians of differing profiles consists in the active, steady monitoring of the state of health of individuals whose condition requires team observation.

Especial attention must be devoted to the use of the method of specialized district center, which makes it possible to normalize the workload of physicians of different specialties, eliminate duplication of effort, and render timely consultation. Specialists must know the people in given districts. In conclusion, it should be noted that further development of mass health screening of the entire population is irrefragably linked to improvement of specialized care, which consists in the following: (1) an in-depth analysis of the size of contingents of patients with a given pathology on the basis of epidemiological studies; (2) the development and introduction of effective methods for prevention, early diagnosis, treatment, and rehabilitation of patients of a given profile, based on the prospect of the growth of the number of patients with their active identification; (3) the introduction of medical equipment, instruments, and devices for identifying disease and the use of the computer to manage the screening of patients of given profiles on the basis of data bases and banks; (4) and the provision of a continuity of operation among all the components of the health care sector through the creation of functional treatment-and-prevention and academic-and-scientific associations and specialized centers in order to raise the medical, social, and economic effectiveness of mass health screening of the entire population.

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Characteristics of Illnesses With Temporary Work Disability in a Clinical Group

18400040b Moscow ZDRAVOOKHRANENIYE ROSSIYSKOY FEDERATSII in Russian No 4, Apr 88 pp 15-17

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[Text] Illnesses involving a temporary work disability (ITWD) are an important criterion of the health of workers and reflect the effectiveness of treatment-and-prevention measures.

The skilled clinical observation that the workers of industrial enterprises undergo, particularly by shop physicians, is of great importance[1,2]. Meanwhile, there are still many difficulties and deficiencies in the service provided to individuals by shop physicians' sections (such as insufficient scope of examinations, poor arrangement of consultations with other specialists, low quality of treatment measures, and discrepancies in diagnoses)[3,4].

The purpose of this report is to summarize the experience in the clinical observation of individuals working at a large artificial leather combine by a team of shop physicians and consulting specialists from the treatment departments of the medical institute.

The Kalinin Iskozh Combine is a part of the light industry sector, although a large amount of chemical substances harmful to the human body are used in its production technology. The medical service for the combine's workers consists of a polyclinic and two medical aid stations that operate on the shop principle.

The figures for ITWD for individuals at this enterprise were rather high, at 110-120 cases and 1200-1300 days per 100 workers (data from annual reports of the polyclinic).

In order to improve the quality and effectiveness of the clinical care at the shop sections, an in-depth study was undertaken of the state of health and morbidity for 190 clinical patients, which constituted nearly 50 percent of all patients being treated under clinical observation. In addition to thorough questioning and objective examination of each patient, ITWD data were copied from disability records and outpatient medical charts (Form 025-u) for 1984-85, and control clinical observation charts (Form 030-u) were analyzed. Additional studies of some of the patients (about 15 percent) were performed in outpatient and hospital conditions.

As a result of an in-depth examination of the clinical group by a team of medical-institute consultants and shop physicians, earlier diagnoses were completely changed in 14 percent of patients, refined in 42 percent, and confirmed in 44 percent. More often, a discrepancy in diagnosis was observed with the differential diagnosis of ischemic heart disease and hypertension, especially when occurring with cardialgia. Discrepancies in diagnosis were rare in rheumatic heart disease, peptic ulcers of the stomach and duodenum, and liver diseases.

The greatest number of ITWD cases among clinical patients in 1984 was in the group of those suffering from illnesses affecting the respiratory organs and the circulation system. In terms of the number of days of work lost, patients with illnesses affecting the respiratory and digestive organs were first. The length of disability per case was greatest in illnesses affecting the urgenital system and the digestive organs (see the table).

Comparative Indices of Temporary Work Disability in a Clinical Group of Patients

Class or group of disorders, individual diseases	Temporary work disability: Number of cases per 100 patients		Temporary work disability: Number of days per 100 patients		Average length of disability, in days	
	1984	1985	1984	1985	1984	1985
Nervous system and sensory organs	127.0	129.7	1435	1197	11.3	9.2
Circulatory	126.8	109.8	1461	1135	11.5	10.3
Hypertension	136.5	120.6	1574	1262	11.5	10.5
Ischemic heart disease	118.2	72.7	1063	1100	9.0	15.1
Chronic rheumatic heart disease	91.7	83.3	1101	1183	11.9	14.2
Respiratory organ disorders	187.5	131.3	1843	1325	9.8	10.1
Digestive organ disorders	77.8	66.7	1574	1088	20.2	16.3
Liver and bile ducts	100.0	125.0	1925	2075	19.2	16.6
Urogenital system	69.2	61.5	1430	823	20.7	13.3
All observed patients	121.0	103.6	1523	1176	12.5	11.4

With thorough questioning and examination of the patients, it turned out that most of them do not have good work and rest habits, and they are not well-versed in the sociohygienic aspects of a healthy lifestyle. Individual risk factors, or a combination of them, for a major illness were identified in some 80 percent of the patients:

unbalanced or unsound diet, lack of exercise (hypodynamia), overweight, family history, psychoemotional stress, smoking, alcohol consumption. More than 30 percent of the patients were treated on an outpatient basis irregularly, and that only during the acute phase of an illness. In connection with this, a large health-education campaign was conducted with all of them to encourage this contingent to adopt a healthy lifestyle. Of great importance was the fact that consultations on the above matters bore the nature of psychotherapy performed by expert specialist-consultants. Corrections in the treatment and examination of the patients were made on the basis of the change in diagnosis. Sports activities were made accessible, and appropriate literature was offered to many patients in the form of instructions, brochures, and the the magazine Zdorovye [Health]. Some of the patients were treated in the plant's clinic and in sanatoria. When necessary, patients were sent for treatment at a hospital. Every patient was given a specific date for a consultation with a physician right on the production premises. For the most part, shift change times, breaks, and nonworking hours convenient for the patient were used for this.

A comparison of ITWD indices for two adjacent years (see the table) indicates a drop in the number of cases per 100 patients in the study group (from 121 to 103.6), in number of days of ITWD per 100 (from 1,523 to 1,176), and in average length of disability per case (from 12.5 days to 11.4). The greatest drop in ITWD was noted in illnesses involving the circulatory system—from 126.8 cases to 109.8. Among those with circulatory system disorders, a substantial drop took place in ischemic heart disease (from 118.2 cases to 72.7 per 100 patients under clinical observation for the disease). In other classes and nosological forms of disease, reductions were less substantial.

ITWD involving respiratory organ problems, in spite of the drop in its figures, remains comparatively high, with a relatively short average length of case (10.1 days). This can be explained by the activation of the inflammatory process in the bronchi that is due to seasonal acute viral respiratory diseases.

Thus, as a result of corrections in the diagnoses of illnesses among clinical patients and differential treatment-and-prevention measures that corresponded to the new diagnoses, ITWD was reduced somewhat. An important feature of the prevention work is not simply the corrected diagnoses, but also the work up of an entire complex of treatment-and-prevention, health, and socioeconomic measures performed by medical institutions. All this facilitates purposeful clinical work, the quality and volume of which brings about a reduction in the loss of work from temporary disability at industrial enterprises.

This indicates that consultation work performed at an industrial enterprise by specialists from medical institutes raises the quality of the diagnostic work done for outpatients and helps to improve the clinical care provided by shop physicians and to raise their skills.

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Genetic Counseling Center Planned for Ukraine

18400041 Moscow IZVESTIYA in Russian
28 Sep 88 p 1

[Article by S. Tsikora, IZVESTIYA correspondent, Kiev: "Genetics Warns"]

[Text] Alas, the present state of affairs does not make us happy. Here is information received at the UkSSR Ministry of Health. In the Ukraine alone almost 100,000 virtually incurable people receive a full state allowance in special boarding houses. The annual increase in patients suffering from hereditary diseases amounts to 10,000 to 12,000 in the UkSSR.

"In our opinion, it is possible to stop the development of this phenomenon, which, unfortunately, is observed in all the country's regions, by only one method—prevention and the establishment of a special service," A. Serdyuk, UkSSR first deputy minister of health, said. "Seven interoblast medico-genetic centers now operate in the Ukraine and consultation offices have been opened. They annually provide help for about 80,000 patients. This is very little if we take into consideration that congenital and hereditary diseases have risen and occupy an ever more significant place in the structure of infantile mortality. Chronic patients suffering from hereditary diseases occupy 20 percent of the beds in children's infirmaries and one-third of the places in hospitals for adults. We set the task of opening medico-genetic centers in every oblast in the very near future and of having medico-genetic offices in all big cities."

It will not be easy for Ukrainian medical men to realize their intentions. From the further talk with A. Serdyuk it has become clear that to date the republic does not have either the necessary number of specialists nor the necessary equipment. The country's higher medical educational institutions as yet do not train geneticists. Nor does such a specialty appear in the tables of organization of medical institutions.

A course in medical genetics is now being urgently introduced in the republic's higher medical educational institutions and practicians will undergo training in advanced training institutes.

The problems of equipping established medico-genetic centers are also very complex. A large number of chemical reagents and a great deal of equipment is needed, but they are not produced by the domestic industry. It was decided to buy them abroad both by foreign trade organizations and with the currency funds earned by enterprises.

"To date genetic diagnosis is the most expensive type of medical examination," A. Serdyuk said further. "Therefore, we will give it primarily to women getting ready to become mothers and to children. Subsequently, most young people getting married will undergo such an examination."

The geneticist can determine with a great degree of reliability whether a child will be healthy or sick.

Experience and Prospects in the Use of Computer Technology and Communications in the Information and Reference Service on Drugs

18400050 Moscow FARMATSIYA in Russian No 3, May-Jun 88 pp 1-4

[Article by O. A. Volkov, V. F. Martynenko, and V. Ya. Yermakova, Main Pharmacy Administration of the USSR Ministry of Health, All Union Scientific Research Institute of Social Hygiene and Health Care Management imeni N. A. Semashko, All Union Information Bureau in the USSR Ministry of Health, Moscow]

[Text] Since 1970, the country's pharmacy service has been using a program that computerized administrative processes through the creation of the computerized Podsistemy GAPU [Subsystems of the Main Pharmacy Administration], which is an integral part of the main ASU, called Zdravookhraneniye [Health Care].

The primary function and the set of tasks performed by the Podsistemy GAPU—management of the drug supply—forms the basis for the development and creation of computerized information retrieval systems (CIRS) and reference information systems (RIS) for various levels: the Union, republic, oblast, and city levels, including the primary health care chain (pharmacy-polyclinic-hospital).

The development of information retrieval and reference information systems proceeds along the following lines: provision of drugs, availability of drugs in city pharmacies, and the drug itself.

The CIRS Lekarstvo is designed to help the physician choose the correct drug for a given purpose, to ensure safety in drug treatment, and to use a wider assortment of drugs available in the pharmacy, with a minimal expense of time in the information search.

The reference file (a computer data bank) must be comprehensive and standardized in structure and content. Thus, according to the specifications stipulated for these purposes by the All Union Scientific Research Institute of Pharmacy, the data bank must include the necessary information on drugs, specially grouped according to chemical, pharmacological, production, and other criteria. The bank must reflect detailed information on the indications and contraindications of drugs, a complex assessment of drug-drug interactions, and a list of domestic and imported preparations and preparations taken out of production. Reference information that is necessary for a search, such as technical standards, is important: disease diagnosis and the drug therapy recommended for it.

On the whole, the information must be consolidated in a branch reference collection on drugs, which should be created by the All Union Information Bureau in the USSR Ministry of Health.

The CIRS Lekarstvo is designed for specialists in treatment and prevention institutions and in pharmacy institutions—which includes pharmaceutical information offices and reference bureaus—and administrative specialists and researchers.

The system must also include reference data for serving the public, including information on drug expiration dates, home storage instructions, and pharmacy dispensing instructions. The system is constantly updated with changing information on the availability of drugs in city pharmacies.

The country's first computerized RIS on the availability of drugs in city pharmacies was created for the people in Riga. It was developed on the basis of computerized accounting of the movement of drugs in pharmacies and at the pharmacy warehouse and of inventory stocks. It operates when data are corrected for the sale or delivery of preparations to the pharmacy system. At present, the system is being improved with the use of video terminals.

In recent years, an information retrieval system developed in Ryazan—known as Managing the Movement of Drugs in the Interhospital Pharmacy—has received a good deal of publicity. This subsystem, which is meant for use by physicians and druggists, enables tracking of arrivals, sales, inventory, and rejected drugs. It also enables the user to make recommendations on priorities for dispensing existing stocks of drugs in the pharmacy in limited quantities and on compiling monthly and annual orders for drugs and to issue other reference information. The subsystem is run on a promising hardware variation of the SM-4 minicomputer.

A new approach in the creation of the CIRS Lekarstvo and the RIS on the availability of drugs in the pharmacy system for treatment and prevention institutions, pharmacy institutions, and the urban population is being taken by the Main Pharmacy Administration and the Republic Information and Computer Center in the Moldavian Ministry of Health, in conjunction with the

Kishinev Medical Institute and the Kishinev ASU Design and Drafting Bureau of the USSR Ministry of Instrument Making, Automation Equipment and Control Systems. The characteristic features of this work consist in the fact that the CIRS system is aimed at handling exchanges of information between the pharmacy and the polyclinic and is built on a standardized design already implemented (the Gomel variation using ES computers). Data processing is done on an SM-4 minicomputer with video terminals. This particular development is in the experimental stage of introduction at the country's first training and production pharmacy in Kishinev. Three types of reference information are generated in the subsystem in the first stage: information on the availability of drugs in the pharmacies, data that can be gotten by the public on Kishinev's pharmacy facilities through the city telephone service, and information on a given drug preparation.

Of interest is the experience garnered in setting up the Minsk City Pharmacy Reference Bureau, which is equipped with five SPS-10/20 message exchanges, telephone and headset communications with operators, and a counting device for determining the number of calls. The SPS-10/20 makes it possible for two operators to use a unit at the same time and allows monitoring of the operator's responses. An experiment is being planned for the creation of a special cost-accounting team of pharmacists of this reference bureau. In all, six such reference bureaus have been set up in Belorussia.

Before the reorganization of the reference service, four reference bureaus in Minsk handled a maximum of 1,300 calls; now, after the reorganzation, they handle as many as 6,000 calls.

Specialists from the All Union Scientific Research Institute of Pharmacy and the Main Pharmacy Administration of the BSSR Ministry of Health have drawn up the Provisional Position on the Pharmacy Reference Bureau With Automatic Telephone Communications.

The reference service in the pharmacy system of the GAPU of the UkSSR Ministry of Health has undergone considerable development since the creation of the Aist system in Sevastopol in 1976. At present, based on requirements specifications, a working draft called the "Information Retrieval System for the Receipt of Medical Goods at the Pharmacy Base and the Pharmacy Network" has been developed within the framework of the subsystem Planirovaniye for drug supply and control of the pharmacy facilities of the republic. The draft calls for the implementation of centralized multichannel reference information bureaus that use microcomputers whose memories contain data on changes in drug assortment and information on, for example, pharmacy facility locations in a city.

The laboratory of the scientific organization of labor and management of the GAPU of the UkSSR Ministry of Health is doing focused work in the area of reequipping the republic's information service.

In 1985, computerized multichannel reference information bureaus were set up in Lutsk, Chernovtsy, and Uzhgorod. In a number of oblasts in the Ukraine, organization of this service entered a second stage in cities under rayon jurisdiction. Telephone information and reference bureaus were opened in cities such as Yevpatoriya, Yenakiyevo, Kramatorsk, Krasnodon, and Lisichansk.

Before completing the installation of equipment and the installation and set up of computer hardware in the centralized computerized multichannel reference information bureau of Kiev, experimental use is being made of a working system based on the Iskra-555 computer complex of the laboratory of scientific organization of labor and management of the GAPU of the UkSSR Ministry of Health.

Step-by-step restructuring of the reference information service is also taking place at present in a number of large cities and oblast centers of the KaSSR and the AzSSR, in certain oblasts of the RSFSR (Ivanovo, Novosibirsk, for example), and in other union republics.

A promising variation of the RIS involves the combination of a drug information retrieval system and the pharmacy reference service that uses city telephone lines; the consolidation of pharmaceutical information offices or information departments and reference bureaus; and the creation of information bureaus located right at the pharmacy warehouse.

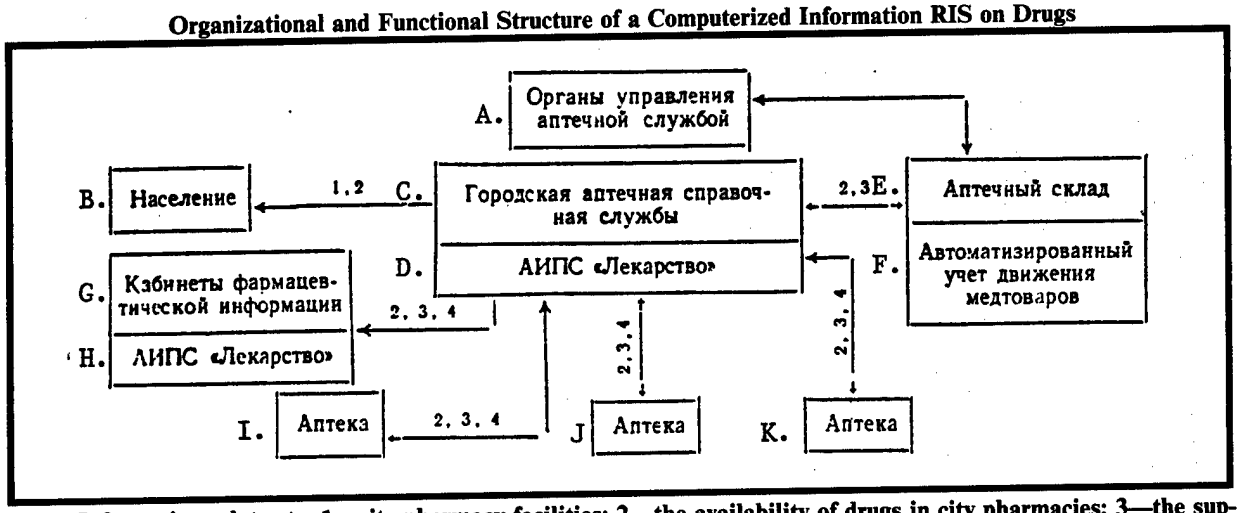
The role of the information service is growing more with the introduction of the set of interrelated tasks (SIT) in the computerized subsystem for the planning of drug provision and the management of the country's pharmacy service at all levels.

In the 11th Five Year Plan, the USSR Ministry of Health GAPU, the All Union Scientific Research Institute of Pharmacy, and the USSR Ministry of Health's All Union Scientific Research Institute of Social Hygiene and Health Care Management imeni N. A. Semashko, in conjunction with the GAPUs of the health ministries of the RSFSR and LaSSR and the corresponding republic computer information centers, developed a SIT Podsistemy GAPU that performs five sets of tasks: planning current levels of need for drugs and medical goods, monitoring planned deliveries of medical products, managing drug stocks, processing statistical accounts, and forecasting growth indices for the pharmacy system.

An RIS involving the status of the drug supply to the public and to treatment and prevention institutions has been created on the basis of the SIT Podsistemy.

Such systems must be developed at various levels in the pharmacy administrations in order to improve the day-to-day management of the drug supply.

Organizational and Functional Structure of a Computerized Information RIS on Drugs



Note. Information relates to: 1—city pharmacy facilities; 2—the availability of drugs in city pharmacies; 3—the supply to the public and to treatment and prevention institutions; 4—specific drugs. The service uses the computer hardware (mini- and microcomputers and monitors) of computer centers and communications systems, including city telephone networks.

Key: A. Pharmaceutical Service Administrative Departments—B. Population—C. City Drug Information Retrieval System—D. CIRS Lekarstvo—E. Drug Warehouse—F. Computerized Accounting of the Movement of Medical Goods—G. Pharmaceutical Information Offices—H. CIRS Lekarstvo—I. Pharmacy—J. Pharmacy—K. Pharmacy

An example of such an approach is the development of a computerized workplace for pharmacy administration specialists. Such a system is being created in the Leningrad gorispolkom and the GAPU of the UkSSR Ministry of Health.

The creation of the RISs examined in this article is based on computerized tracking of the movement of drugs and of inventory at the pharmacy warehouse and in the pharmacies and on a reference information collection concerning drugs (see the diagram). Without these component parts, the RISs cannot possibly function.

The directions noted here on the creation of the CIRS Lekarstvo (on the availability of drugs in city pharmacies and on the status of the drug supply) hold a great deal of promise for raising the level and quality of the provision of drugs to the public and to treatment and prevention institutions.

UDC 615.38.002.3:[002.6:65.011.56

Development and Management of Automated Donor Registries at Blood Transfusion Centers

18400035f Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 5, May 88 (manuscript received 25 May 87) pp 44-47

[Article by I. B. Sushchenko, doctor of medical sciences, T. I. Inyakina, and L. A. Kalinina, Institute of Biophysics and Blood Transfusion Station, No 6 Hospital, USSR Ministry of Health, Moscow]

[Abstract] One of the most important problems encountered in the management of blood transfusion centers and services lies in monitoring and controlling blood donors, both volunteers and those seeking remuneration. An effective means of exercising such control and ensuring that available donors are used efficiently and in a manner compatible with good health practices must rest on an automated donor registry. A database of this type would include all the pertinent information on an individual donor, including the frequency of donations, general medical data, immunologic information including histocompatibility profile, and a record of immunizations. A unified donor profile may be created on the basis of the important donor information, and a coding system devised for identification and tracking of donors to meet medical emergencies. A system of this type has already been developed which relies on SM-4 minicomputers and utilizes DIAMS-2 software. References 6 (Russian).

UDC 378.661

Some Problems in Medical Colleges (VUZ)

18400038b Moscow ZDRAVOOKHRANENIYE ROSSIYSKOY FEDERATSII in Russian No 4, Apr 88 (manuscript received 7 Apr 87) pp 35-38

[Article by L. N. Ternovskiy, A. A. Dregalo, and V. A. Ternovskaya, Arkhangelsk Medical Institute, RSFSR Ministry of Health]

[Abstract] A survey of Arkhangelsk students showed that, of 40 professions, medicine was the leading one. That city's medical college ("institute") has a good reputation and provides a satisfactory basis for teaching future physicians. However, there are several problems,

the most important of which is that the students do not know how to study. Next, the mix of student body ranges from excellent candidates coming from pre-med schools to average and poorer candidates from the working cadres and from demobilized individuals. Yet, after the first year a sort of averaging is observed between these extremes. To some extent this is good in that the poor students show improvement but also it is bad in as much as the real talented ones do not seem to excel and the students do not commit themselves 100 percent to their task. Some students work outside the school in order to make more money for extravagant, prestigious items; some are married and have families to support. Neither situation contributes to good study habits. This problem goes beyond school's responsibilities. Other social institutions must make it clear that the principal task of a student is to study. Some responsibility for this must fall on the staff which should transmit to the student body the basic principles of life and social experience, the bridging of generations.

Insufficient Monitoring of Nitrate-Contaminated Produce in Kirghizia

18400044 Moscow SOTSIALISTICHESKAYA INDUSTRIA in Russian 27 Jul 88 p 1

[Article by V. Yurlov, special correspondent, Frunze]

[Abstract] Nitrate-contaminated produce in Kirghizia has become an acute problem in Kirghizia, affecting both produce grown on private plots and that supplied by state and collective farms. This stems from a blatant and virtually uncontrolled use of nitrate fertilizers and ineffective administrative monitoring and control measures. As a result, spot checks have shown that too many produce samples exceed the maximum permissible levels of nitrates, by factors ranging from two- to five-fold. Such exposure to excessive levels of nitrates in the diet may be a factor for the increasing cancer morbidity in Kirghizia, particularly in the case of gastric and hepatic malignancies. Despite some talk about improving the effectiveness of health services in monitoring and controlling dietary nitrates in Kirghizia, the situation remains serious with no clear-cut improvements in sight.

Public Health Restructuring in Kirghiz SSR

18400045 Frunze SOVETSKAYA KIRGHIZIYA in Russian 31 Aug 88 p 1

[Interview with Bekmurza Ismailov, Kirghiz SSR Minister of Health, conducted by Yuriy Blyum, correspondent KirTAG [Kirghiz Telegraphic Agency]

[Abstract] One of the key problems in Kirghizia in the public health sphere lies in the fact that the number of available hospital beds is not keeping pace with the growing population, with this parameter falling to 118.6 beds per 10,000 population, versus an All-Union average of 130. As a result, future years will see a 5- to 6-fold increase in health funding over that available in the current 5-year plan. However, more importantly, there will be an increase in emphasis placed on individual initiative in rendering health service, and the responsibilities and authority of local government bodies will be expanded to ensure greater responsiveness to local needs. The educational system will be overhauled to improve the quality of training that medical students receive, and the scope of postgraduate medical education shall undergo serious evaluation with a view toward establishing an institute for advanced training of physicians. In addition, considerable attention must be accorded to improving physician-patient relationships and in rendering the entire health profession more responsible to the needs of Kirghiz citizens. Finally, steps must be taken and will be taken to enhance self-esteem and professionalism among the medical workers in Kirghizia.

Psychological and Medical Studies During Polar Expeditions

18400068a Moscow PSIKHOLOGICHESKIY ZHURNAL in Russian Vol 9 No 3, May-Jun 88 pp 68-71

[Article by N. V. Krylova, T. Ye. Kuznetsova and I. B. Solovyeva, Institute of Psychology, USSR Academy of Sciences, Moscow; 2nd Moscow Medical Institute

[Abstract] A brief survey is presented of some Soviet studies conducted in the course of polar expeditions in both the Arctic and Antarctic regions with the purpose of delineating medical and psychological parameters affecting performance efficiency. The monitoring was conducted with a female crosscountry skiing team (Metelitsa) under the auspices of the Institutes of Biomedical Problems, Psychology,and of Biophysics of the USSR Academy of Sciences. The expeditions were conducted during the polar day and lasted 15 to 25 days. Generally, skiing was conducted during the nighttime while daytime was reserved for resting. Thirty minutes of racing was alternated with 5 min rest periods during a 8-10 h 'workday.' The psychological and medical assessments conducted on the team members identified collegiality as a key feature of a successful expedition, supported by such individual characteristics as a sense of humor, tolerance, responsibility, equanimity and so forth. The various physiological parameters remained within normal limits, with some initial lability of the cardiovascular system during the first few days of an expedition. In general, adaptation to extreme conditions prevalent in the polar regions reflected individual experience and degree of physical training and mental conditioning. The information that was gathered demonstrated that collectives such as Metelitsa may serve as a model system for assessing performance of occupational groups under extreme environmental conditions. References 2 (Russian).

Psychological Assessment of Occupational Fitness

18400068b Moscow PSIKHOLOGICHESKIY ZHURNAL in Russian Vol 9 No 3, May-Jun 88 pp 93-101

[Article by V. M. Zvonikov, V. A. Ponomarenko and V. I. Tsuvarev]

[Abstract] Criteria entering into psychological evaluation of occupational fitness were analyzed in terms of factors applicable to successful test pilots. The study was based on questionnaires, analysis of publications, psychometric tests, and personal interviews. The three most important characteristics were identified as actual job performance, careful planning and job analysis skills, and social awareness and a high-developed sense of responsibility. The demonstration of analytical skills was felt to be one of the key factors in differentiating individuals qualified to be ordinary pilots from those qualifying as test pilots, with the later demonstrating a scholarly' mindframe necessary for evaluation of test results. The successful test pilots showed early maturation of their occupational interests and were highly motivated to excel and serve society. The psychometric studies revealed highly advanced cognitive skills and abilities in comparison with other classes of pilots. On the basis of these observations a test battery was developed for assessing occupational fitness for test pilots, encompassing 16 methods that evaluate 63 psychopsychological components in the test pilot training programs designed to prevent eventual onset of occupational arrogance, intolerance, 'bonapartism,' and egotism. References 14 (Russian).

Enzyme Immunoassay for Detecting Antigen and Antibodies for Human Immunodeficiency Virus and Its Use for Serological Survey of Various Population Groups

18400049a Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 3, May-Jun 88 pp 294-298

[Article by V. M. Zhdanov (deceased), E. V. Karamov, S. A. Arakelov, I. A. Rudneva, Ye. S. Ketiladze, V. M. Stakhanova, N. A. Malyshev, and I. L. Alekseyeva, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Text] The first cases of AIDS (acquired immune deficiency syndrome) were recorded in 1981, in the United States.[5] The infection spread widely over the next six years, and at present it has been described in 110 countries of the world, diagnosed in 42,404 individuals as of 11 March 1987. The agent of AIDS is a new type of retrovirus isolated in France in the Pasteur Institute (Paris)[3] and in the United States in the National Cancer Institute (Bethesda).[4]

The principal and most widely used method for identifying individuals infected with the human immunodeficiency virus (HIV) is enzyme immunoassay (EIA) of antibodies for specific proteins in blood serum.[6] Other laboratory tests include isolation of the virus or detection of its components (antigens, nucleic acid, reverse transcriptase).

The commercial test systems now being manufactured make it possible to determine only the antibodies for HIV. In our own work to create a domestic IEA diagnostics test, we strived to obtain a modified method that would provide broader diagnostic opportunities and that would be capable of determining not only HIV antibodies, but also HIV antigens. The purpose of the work was also to screen the blood sera of various population groups (primarily groups with an elevated risk of infection) for HIV antibodies.[1]

Material and methods. Organon (Holland) and Abbott (USA) commercial test systems for determining HIV antibodies were used in the work. A total of 5,743 individuals were tested.

Results and discussion. We obtained the HIV antigen used in the enzyme immunoassay by growing an EVK lymphoblastoid cell line produced at the Institute of Virology imeni D. I. Ivanovskiy on the basis of a collection of human lymphoblastoid cells existing in an immunochemistry group. The sensitive cell line was infected with an HIV isolate taken from an individual with lymphoadenopathy.[2] The EVK line cell population that produces HIV bears markers for early T cells. Karyologic analysis of the EVK line with the C stain method indicated that the cells do not have marker chromosomes, and the modal class for cells of this line has 46 chromosomes.

The EVK cells were grown on an RPMI-1640 medium to which a 10 percent embryonal calf serum, 600 μg/ml glutamine, and 160 μg/ml gentamycin were added; the growth was in a CO_2 incubator at 37°C, with 4.2 percent CO_2. The seed dose was 5-8 x 10^5 cells/ml. The cells were grown to a density of 1.8-2.3 x 10^6 cells/ml. The culture was passivated every fifth or sixth day. Cell suspensions achieving maximum growth density were centrifuged at 1,000 rpms for 10 minutes. After concentration and purification, the supernatant liquid containing the virus was used as the HIV antigen, and the cell precipitate was diluted in a fresh growth medium to the appropriate cell concentration and further passivated.

Forming the basis of the diagnostic test system that we developed were HIV antibodies (immobilized on the surface of polystyrene boards and conjugated with peroxidase of horse radish) and the HIV antigen.

The Organon (Holland) commercial test system was used to investigate the serum containing the HIV antibodies. This test was used to select a patient's serum with a titer of 1:20,000. The conjugate with the peroxidase of horse radish was prepared on the basis of the antibodies (immunoglobulin fraction) obtained from this serum. The specific activity of the conjugate was checked with the boards with the immobilized HIV antigen from the Organon test. Unlike the currently manufactured commercial tests, which use an antispecies conjugate, the method we are developing is based the principal of concurrent analysis, with the use of an antiviral conjugate, which makes it possible to test the sera without preliminary dilution.

The purified HIV antigen was tested in a "sandwich" reaction on the boards with the immobilized HIV antibodies. With the completion of the sandwich reaction, we selected the optimal conditions of analysis. In stage I we determined the optimal concentration of the antibody preparation for adsorption on solid phase. For that we immobilized HIV antibodies overnight at room temperature from solutions of varying concentration in a 0.05 mole/dm^3 carbonate buffer, at pH 9.5, on boards made by the scientific production association Medtekhnika (Moscow), and we analyzed the HIV antigen in a culture liquid inactivated with a detergent (0.1 percent triton X-100) and ultrasound, with the use of a conjugate diluted 1:1000 in a 0.05 mole/dm^3 phosphate buffer, at pH 7.2, containing a 5 percent solution of cattle serum, 2 percent normal human serum, and a 0.1 percent solution of detergent (triton X-100). For verifying the specificity of the analysis, those same HIV antigen samples were tested in duplicate with a conjugate containing a serum with HIV antibodies in a titer of 1:2000 instead of normal human serum (neutralization test). The results of the analysis were evaluated in terms of the degree of suppression of positive staining in the neutralization test, which was expressed in the form of an N/A ratio, where N is the optical density of the positive stain in the analysis with the conjugate containing the normal serum, and A is the optical density in the analysis with

the conjugate containing human anti-HIV serum. The maximum sensitivity of the analysis is achieved with the adsorption of the antibodies on the solid phase from a solution with a concentration of 2-4 μg/ml. Increasing the concentration to more than 10 μg/ml leads to a reduction in sensitivity as a result of the diminished effectiveness of antigen binding and the growth of background staining.

Later, using the N/A ratio as a criterion, we optimized test system parameters such as incubation time with antigen and with conjugate (2 and 1.5 hours, respectively) and working dilution of the conjugate (1:1000).

Analysis for identifying HIV antibodies in blood sera was conducted on the basis of the test system we developed by means of blocking the sandwich reaction. For that, into the cavities of a board sensitized by HIV antibodies we placed, one after the other, 100 μl HIV antigen (stage I) and 10 μl of the serum under study (without preliminary dilution) and 90 μl conjugate (stage II). Each stage was accompanied by incubation and washing. After that, we used the specific conjugate (without the neutralizaton test) to conduct the above-described analysis for HIV antigen. In evaluating the results, we considered a sample positive if it caused a 70 percent or greater suppression of staining, by comparison with the negative controls (which did not contain HIV antigen).

In order to conduct the analysis for identifying HIV antibodies, the antigen sample must contain enough of the antigen to assure consistent optical density values for studying the results of the reaction. Deviation in the analysis of negative sera cannot exceed 20 percent. An excessive amount of the antigen in the sample for conducting the analysis for HIV antibodies leads to a reduction in the sensitivity of the method, since in this instance a considerable number of antibodies are required for reliable neutralization. The optimal antigen concentration is one that ensures an optical density of between 0.5 and 1.5 as a result of the reaction with the negative sera.

We compared the test we developed with the commercial Organon test for identifying HIV antibodies. Samples were prepared with various concentrations of antibodies by means of diluting in batches a positive serum in the normal serum of a healthy donor. The results of the experiment are presented in Table 1. The samples—which were positive in the test system of the Institute of Virology, and negative in the Organon test—has a low concentration of specific antibodies as a result of the high degree of dilution of the positive serum. Since the conditions for administering the Organon EIA require preliminary dilution of the serum to 1:100, that test system does not enable identification of HIV antibodies if they are of low concentration in native serum. Thus, one of the advantages of the method we developed is the possibility of studying native sera without preliminary dilution, which makes the method highly sensitive.

Table 1: Results of the study of blood serum samples in different test systems

Sample no.	Optical density, units op. dens.		Results	
	Organon system[1]	Inst. Virology system[2]	Organon system	Inst. Virology system
1	1.64	0.05	+	+
2	1.02	0.06	+	+
3	0.64	0.06	+	+
4	0.42	0.08	+	+
5	0.23	0.07	+	+
6	0.14	0.09	-	+
7	0.08	0.09	-	+
8	0.06	0.12	-	+
9	0.07	0.21	-	+
10	0.06	0.39	-	-
11	0.06	0.62	-	-

[1]Threshold value, 0.20. [2]Threshold value, 0.26.

The test we developed has been used in the clinical department of the Institute of Virology to screen the blood sera of high risk groups for HIV antibodies. From September 1986 through April 1987, a total of 5,743 individuals were examined.

A total of 3,800 studies were done with the Institute of Virology test system, 1,000 were done with the Organon system, and 100 were done with the Abbott system.

All the blood sera were examined at the same time for the presence of HBsAg with ROPGA [not further identified] and radioimmunoassay (RIA). In all the groups, the number of positive results did not exceed 1.5-2.0 percent; among the blood donors, however, we examined individuals with HBsAg in a special way. Those individuals were included in the group of HBsAg carriers. That group included pregnant women who were carriers of HBsAg (87 individuals) from the Korshinskiy Rayon of UzSSR.

A great many studies were done with individuals from Moscow. The blood donors were from various regions of the USSR: Moscow (333), Perm Oblast (173), Kazan (29), Tallin (100), Moldavian SSR (70), and Baku (204).

Tested for HIV antibodies were individuals belonging to high risk groups for HIV infection: medical personnel (surgeons, procedures nurses, and regular nurses) from the Perm Oblast; drug addicts (primarily those who take drugs intravenously); homosexuals; asocial elements (prisoners and prostitutes); individuals with venereal, oncologic, or somatic diseases or tuberculosis; and patients at psychiatric clinics (chronic alcoholics and the mentally ill). Viral hepatitis patients include those with acute hepatitis B; non-A, non-B (parenteral) hepatitis; chronic hepatitis (HBsAg-positive); and delta infection. Patients with severe infectious pathology were represented by patients from the reanimation department suffering from serous and purulent meningitis,

meningoencephalitis, sepsis, and severe forms of pneumonia. Among those with immune deficient states were those who were ill with respiratory diseases often and for lengthy periods and those who had generalized forms of herpetic and cytomegaloviral infection.

Among the clinical signs of AIDS are lengthy fevers of unclear origin, lymphoadenopathy, weight loss, lengthy periods of diarrhea, and pneumocystic pneumonia.

The healthy population was represented by residents of Moscow, the Smolensk and Murmansk oblasts, and Moldavia.

The foreign citizens were individuals who had come to the Soviet Union from various countries of Europe, Asia, Africa, and Latin America to study or to work.

The results of the examinations are presented in Table 2.

Table 2: Results of serological screening of blood sera for HIV antibodies

Contingent	Total number screened	Number of positive results
USSR citizens	4898	0
Healthy population	557 (375/182)	0
Blood donors	909	0
HBsAg carriers	279	0
Medical personnel	50	0
Individuals who had gone abroad	58	0
Asocial elements	181	0
Drug addicts and homosexuals	453	0
Patients with clinical signs of AIDS	38 (20/18)	0
Patients with immune deficient states	254 (96/158)	0
Patients with venereal disease	310	0
Patients with severe infectious pathology	266 (124/142)	0
Somatic patients	240	0
Cancer patients	71	0
Tuberculosis patients	386	0
Patients with viral hepatitis	362 (327/35)	0
Patients from psychiatric clinics	464	0
Patients who had received blood transfusions within the last 5 years	20	0
Foreign citizens	845	6
Europe	205	0
Asia	201	0
Africa	341	6
Latin America	98	0
Total	5743	-

Note: The first number in the parentheses represents adults, the second number children.

Among the 4,898 Soviet citizens tested, there was not a single positive result. Of the 845 foreign citizens, HIV antibodies were found in six individuals, from African countries: Uganda (1), Guinea (1), Equatorial Guinea (1), Namibia (1), and Angola (2). Positive sera were tested again, and the results were confirmed with the Organon immunoblotting test.

In five of the six individuals, clinical signs of AIDS were absent at the time of the test. The sixth had been hospitalized in Madrid (Spain) for four months, with an unestablished diagnosis; the patient was brought to the USSR in a state of cachexia and died within three days.

Thus, HIV antibodies were not found in USSR citizens at high risk for infection. The greatest danger is presented by foreign citizens coming from African countries.

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Low Frequency of False Positives in Serological Identification of Human Immunodeficiency Virus Among Groups of Young, Healthy Individuals

18400049b Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 3, May-Jun 88 pp 298-302

[Article by V. M. Zaydes, V. E. Berezin, V. V. Bubnov, S. Yu. Klyushnik, L. I. Korobov, Yu. A. Boshchenko, and V. M. Zhdanov (deceased), Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Text] The problem of false results in the serological diagnosis of AIDS is extremely varied and has no clear solution. A great many such results consist of false positives that are obtained in the study of blood sera in commercial test systems for enzyme immunoassay (EIA), which are set up on the basis of antigens of viral particles. In the United States, the frequency of false positives in a massive screening of donor blood with a first-generation Abbott test system reached 90 percent. According to recently published data, the frequency of false positives in the examination of individuals with acute and chronic diseases has been higher than 97 percent.[5]

As is known, according to established practice, samples yielding positive results with EIA screening must be examined further in so-called comfirmatory [Russian: podtverzhdayushchiye] test systems in order to formulate a conclusive serological diagnosis, and only with another positive result can the sample be declared to contain anti-HIV, and the individual declared to be infected with HIV.

Among the various methods for formulating confirmatory analysis, the immunoblot test is the most widespread method, even in terms of commercialization.[6] In screening several dozens of serum samples of donors and individuals suffering from various acute and chronic illnesses—samples that had produced positive results in Organon Vironostika and domestic EIA test systems—we did not detect a single case of anti-HIV when we used an immunoblot test system that we had developed.[1-4] All these results were in good agreement with data cited earlier on the high frequency of false positives in the screening of sera for anti-HIV with EIA test systems. However, when screening the sera of young people—students at higher educational institutions (VUZes) in Odessa—we unexpectedly found complete agreement in terms of positive results in EIA screening and immunoblot screening, i.e., the absence of false positives. The data we obtained are presented below.

Material and methods. *Screening techniques.* A total of 1,002 foreign students studying at VUZes in Odessa were screened. Five milliliters of blood were taken in sterile conditions from the ulnar vein with disposable syringes. The samples were coded with consecutive numbers at that time. After fibrin clots were removed, the sera were placed in sterile ampules (each sample filled two ampules) and stored at 4°C for one month. The sera were flown in by airplane, and we analyzed them with EIA. Selected samples were then further studied with immunoblot. If a positive result was obtained, the sample was "decoded" so that blood could again be taken from the individual to be rechecked. This allowed for possible errors at the coding stage.

Serological serum studies. A classical two-stage study was done. The first stage involved the Organon (Holland) Vironostika EIA test system; samples declared positive were analyzed again with EIA and then in a confirmatory immunoblot test system (jointly developed by the USSR Academy of Medical Sciences Institute of Virology imeni D. I. and Ivanovskiy and the USSR Ministry of Health Moscow Institute of Viral Preparations). Samples that showed positive with EIA and immunoblot were analyzed again, for which blood was again drawn. In this instance, analysis was limited to EIA. Formulation and consideration of the EIA results were done according to the technical manuals; immunoblot results were examined according to the approved directions on use.

Results and discussion. As early as the initial testing of the sera with EIA, we observed a characteristic feature that distinguished the sera we were studying from those we had studied earlier—sera from donors, from individuals with various acute and chronic illnesses, and from individuals selected on the basis of nonbiological criteria. The feature consisted of an exceptionally low level of "signals" found in most sera (declared negative) and, apparently, partially associated with this circumstance was the relatively high strength of "signals" with sera repeatedly yielding positive results with EIA. In fact, as Table 1 shows, the average optical density of eleven randomly selected negative samples is lower than the company's negative control, and the values a little higher (sera No. 1184 and 1692) are at the level of the negative control. Conversely, the optical densities of the positive samples confirmed by immunoblot are extraordinarily high: their values, as a rule, are higher than the values ascertained with the company's "high positive" serum. It should be emphasized that the results presented in Table 1 are typical for the entire lot of sera.

Table 1: Typical results of serological screening of sera

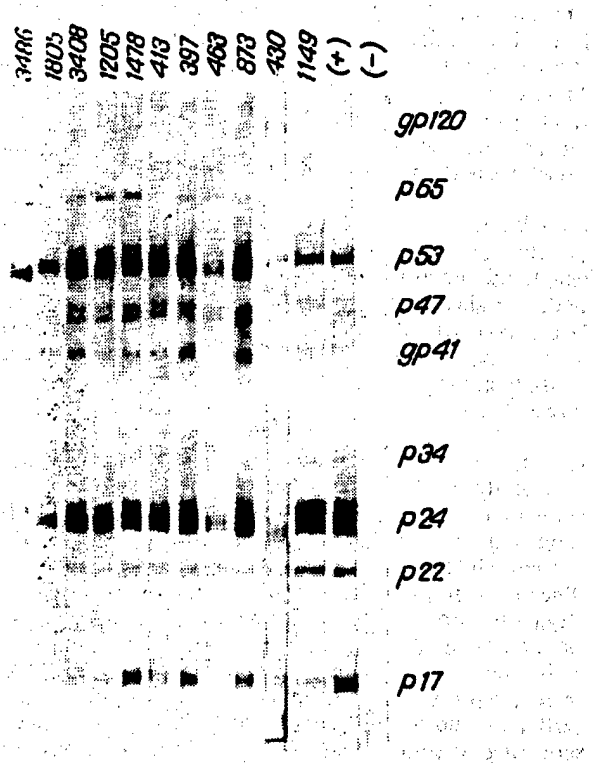
Serum No.	Organon EIA test system: Initial drawing of blood, First determination	Organon EIA test system: Initial drawing of blood, Second determination	Organon EIA test system: Second drawing of blood	Immunoblot study of EIA positives
1184	0.135	-	-	-
1205	1.158	0.675	1.096	Positive
1687	0.106	-	-	-
1692	0.126	-	-	-
1693	0.114	-	-	-
1740	0.112	-	-	-
1805	1.006	0.525	0.890	Positive
2736	0.084	-	-	-
2762	0.094	-	-	-
2804	0.103	-	-	-
3194	0.096	-	-	-
3202	0.110	-	-	-
3203	0.110	-	-	-
3205	0.107	-	-	-
3408	1.160	1.045	1.460	Positive
Control:				
Negative	0.122	0.140	0.173	-
Low positive	0.372	0.211	0.331	-
High positive	0.893	0.620	0.988	-

Note: The optical density is in board cavities at E = 492 nm.

The data in Table 1 also provide a clear idea of the tactics we used in conducting the serological diagnostic testing. The first column of the table presents the results of the uniform study of the initial material with EIA; the second column, the results of retesting of sera declared positive (for that we used the sera from the second ampule—see the section "Material and methods"); the third column, the results of the EIA testing of sera obtained when blood was drawn for a second time; and the fourth column, the results of testing of the same sera with immunoblot.

All eleven serum samples declared positive with EIA were analyzed with a confirmatory immunoblot test. As the figure shows, all the samples meet the criteria for being placed in the category of containing anti-HIV. Most of the samples show rather similar spectra of antibodies, with maxima in the regions of the proteins p53 (pol and gag genes) and p24 (gag gene) and signals of moderate strength in the region of high-molecular glycoprotein gp120 (env gene) of protein p47 (possibly, pol gene) and gp41 (env gene) of protein p34 (pol gene) and proteins p22 and p17 (gag genes). At the same time, one cannot help but notice marked differences in the spectra. Sera No. 1805, 413, and 430 do not produce "signals" in the region of p65 (pol gene), and sera No. 3486 and 463 do not interact with protein p17 and interact weakly with protein p24.

Table 2 shows the regional distribution of antibody carriers (consequently, of individuals infected with HIV). As can be seen, all the carriers are from the African continent (it should be noted that the small number ofscreened individuals from Asia and Latin America lowers the reliability of the results obtained in regard to



Immunoblot study of EIA positive sera

For the immunoblot, we used nitrocellulose strips with immobilized proteins of HIV (series 29). The formulation was done as described earlier.[1-4] Above the tracks are the numbers of the sera under study and the control positive (+) and negative (-) sera.

those individuals). The intracontinental distribution of the serum-positive individuals agrees well with the existing data. The greatest percentage of serum-positive individuals (more than 6 percent) was identified among representatives of Central Africa. It is not out of the question that the figure obtained is elevated because of the comparatively small sample or because of epidemiological features that have not been considered (for example, differences in the "density" of any sort of contact within the different regional groups are possible).

Regional distribution of serum-positive individuals

Region[1]	Number of individuals screened	Number of serum-positive individuals	
		Absolute	Percentage
Africa:			
North	183	0	-
Center	140	9	6.4
East	139	1	0.7
West	347	1	0.3
Southeast	138	0	-
Asia	39	0	-
Latin America	16	0	-

[1]Regions of permanent residence are listed.

Of the eleven identified serum-positive individuals, 10 are men. The prevalence of the men, however, is apparently just a reflection of their overall predominance among those screened as well as among students of foreign descent. The woman in whose blood the HIV antibodies were found is the wife of one of the 10 serum-positive men.

An unusual confluence of circumstances led to the rather rare agreement of results of the anti-HIV serological testing obtained with the traditional solid-phase EIA and the results obtained with immunoblot. The testing of healthy young individuals among whom were a rather large number of individuals with HIV was a deciding factor.

We thank Professor S. S. Marennikov for providing the virus-containing liquid.

Footnote

*The term "podtverzhdayushchiy" is a literal translation of the English term ("confirmatory") that has become established in the literature; actually, the matter at hand involves not so much the confirmation of a diagnosis as it does the formulation of a diagnosis; in fact, the diagnosis of antibody carrier status in the work of A. F. Etkin et al cited above[5] was rejected in 35 individuals who had had a positive result in EIA, but did not belong to a high risk group for AIDS; in accordance with established practice, "unconfirmed" samples are declared to not contain anti-HIV, and their sources are declared to be uninfected with HIV (human immunodeficient virus).[6]

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UDC 616.98:578.828]-092:612.017.1-064-021.5]-07:[616.155.32-008.97:578.828]-078

Detection of HIV Antigens in Lymphocyte Culture of AIDS Patient With Kaposi's Sarcoma From Central Africa

18400033c Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 2, Mar-Apr 88 (manuscript received 13 Nov 86) pp 188-192

[Article by V. M. Zhdanov (deceased), M. I. Parfanovich, N. G. Yaroslavtseva, I. I. Kucherov, N. S. Potekayev, Yu. I. Zimin, and Ye. A. Shuginina, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Cell culture studies were conducted (in the USSR) on a 33-year-old indigenous Central African male, suffering from AIDs [in Russian, SPID] and Kaposi's sarcoma to assess persistence of HIV (human immunodeficiency virus) in the patient's leukocytes. Cocultivation of the patient's cells with leukocytes derived from a healthy donor yielded a culture testing positive for HTLV-III antigen in ELISA tests using Abbott (USA) reagents. HIV was also detected on the surface of cultured lymphocytes by immunofluorescence tests. Finally, the cell supernatants regularly demonstrated reverse transcriptase activity using poly(rA)oligo(dT) templates. References 7 (Russian).

UDC 57.086.83:578.828.083.22

Cultivation of Human HIV-Producing Cells

18400033d Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 2, Mar-Apr 88 (manuscript received 19 Jan 87) pp 192-196

[Article by V. M. Zhdanov (deceased), A. I. Gromyko, F. I. Yershov, D. N. Nosik, M. N. Korneyeva, and N. S. Korsun, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Tissue culture screening trials were conducted with interleukin-2 and poly- and monoclonal antibodies against human interferon to determine whether either factor in isolation or in combination with the other would enhance HIV antigen production by cells with persistent HIV infection. Evaluation of the results obtained with the HUT 102 and H9/IIIB T cell lines showed that treatment of the cells with either preparation had no telling effect on the expression of the HIV antigen. However, when used in combination, i.e., interleukin-2 + antiinterferon antibodies, a 1.5-fold increase in the HIV antigen was noted. These observations indicate the need for more extensive screening studies to identify additional factors that may be even more efficient in enhancing HIV antigen expression, thus transforming such infected cell lines into a ready source of a diagnostic reagent—the HIV antigen—with potentially extensive applications in AIDS diagnosis and blood product monitoring. References 9: 2 Russian, 7 Western.

UDC 578.833.26:578.74

Nonvirion (Soluble) Antigen of Tick-Borne Encephalitis Virus (TBEV)

18400033e Moscow VOPROSY VIRUSOLOGII in Russian Vol 33 No 2, Mar-Apr 88 (manuscript received 12 Sep 86) pp 217-227

[Article by T. S. Gritsun, V. N. Lyapustin, G. G. Karganova, and V. A. Lashkevich, Institute of Poliomyelitis and Viral Encephalitides, USSR Academy of Medical Sciences, Moscow]

[Abstract] Various immunoelectrophoretic techniques were utilized in an analysis of the nonvirion (soluble) antigen (NA) of TBEV, the function of which in viral reproduction remains enigmatic. TBEV was grown in a continuous line of pig embryonic kidney cells, with the analyses conducted on high and low MW structural complexes derived from the cells following detergent treatment. Treatment with nonionic detergents yielded electrophoretically heterogenous protein components of NA, whereas treatment with SDS provided a homogenous fraction. Studies with radiolabeled precursors of carbohydrates, lipids, and RNA led to the demonstration that NA is a membrane-containing ribonucleoprotein complex. Immunoaffinity precipitation on CNBr-activated Sepharose demonstrated that the antigenically specific component of NA was represented by protein NV5 (p93). The disparity in the MWs for NA reported by various laboratories is attributed to proteolytic degradation of NV5 with the formation of a number of proteins (p48, p49) in the course of immunochemical preparation. While the function of NV5 remains unclear, preliminary data indicate that it possesses RNA-polymerase activity. The high antigenicity of NA further suggests its importance in TBEV immunity. Figures 5; references 35: 12 Russian, 23 Western.

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